Chapter
14

Anesthesia for burned patients

Lee C. Woodson, Edward R. Sherwood, Asle Aarsland, Mark Talon, Michael P. Kinsky and Elise M. Morvant

Chapter contents list

Introduction

Continuous improvement in burn care since World War II has resulted in a steady increase in the rate of survival after large burn injury.[1] These improvements have been attributed to aggressive fluid resuscitation, early excision and grafting of burn wounds, more effective antimicrobials, advances in nutritional support, and development of burn centers. Today, most patients with more than 80% total body surface area (TBSA) burned will survive if promptly treated in a modern burn unit with adequate resources. In their study of risk factors for death following burn injuries Ryan et al. identified three variables that can be used to estimate the probability of death: age greater than 60 years, burns over more than 40% of the total body surface area, and the presence of inhalation injury.[2] Mortality increased in proportion to the number of risk factors present: 0.3%, 3%, 33%, or approximately 90% mortality depending on whether zero, one, two, or three risk factors were present, respectively. The incidence of mortality is also influenced by significant coexisting disease or delays in resuscitation. O'Keefe et al. observed an approximately two-fold higher death risk of death in women aged 30 to 59 years compared with men with similar burns and age.[3] Although it has been assumed that very young children are also at increased risk of death from burn injuries, Sheridan et al. found very low rates of mortality in children younger than 48 months who had suffered large burns.[4] Some burn patients develop refractory burn shock soon after injury and cannot be resuscitated.[9]

Major burn injury results in pathophysiological changes in virtually all organ systems. Table 14.1 lists and Figure 14.1 illustrates some of the challenges presented by the acutely burned patient during the perioperative period. In addition to the predictable challenges relating to airway management, monitoring, and vascular access, patient positioning requires close communication and teamwork. Burns involving posterior areas may require turning the patient to the prone position for optimal access (Figure 14.1). Vascular catheters and the endotracheal tube must be secured with confidence and due care given these life lines during patient turning. Several highly informative reviews of anesthetic management for burn surgery have been written during the past decade, each with its own special areas of concentration.[5–7]

Patients suffering burn injuries often require surgical treatment for years after the initial injury in order to correct functional and cosmetic sequelae. Anesthetic management for reconstructive burn surgery presents many special problems[8] but this chapter will concentrate on the care of acute burn patients. The acute phase of burn injury is defined as the period from injury until the wounds have been excised, grafted, and healed.

Modern burn care depends on coordination of a multidisciplinary team including surgeons, intensivists, nurse clinicians, nutritionists, rehabilitation therapists, pulmonary care therapists, and anesthesia providers. Rational and effective anesthetic management of acute burn patients requires an understanding of this multi-disciplinary approach so that perioperative care is compatible with the overall treatment goals for the patient. The current standard of surgical treatment calls for early excision and grafting of nonviable burn wounds, which may harbor pathogens and produce inflammatory mediators with systemic effects resulting in cardiopulmonary compromise. After an extensive burn injury, the systemic effects of inflammatory mediators on metabolism and cardiopulmonary function reduce physiological reserve and the patient's tolerance to the stress of surgery deteriorates with time. Assuming adequate resuscitation, extensive surgery is best tolerated soon after injury when the patient is most fit. However, it must be recognized that the initial resuscitation of patients with large burns results in large fluid shifts and may be associated with hemodynamic instability and respiratory insufficiency. Reynolds et al. reported that more than half of deaths after burn injuries occur due to failed resuscitation.[9] Effective anesthetic management of patients with extensive burn injuries requires an understanding of the pathophysiological changes associated with large burns and careful pre-

TABLE 14.1 PERIOPERATIVE CHALLENGES IN THE ACUTE BURN PATIENT

- Compromised airway
- Pulmonary insufficiency
- Altered mental status
- Associated injuries
- Limited vascular access
- Rapid blood loss
- Impaired tissue perfusion due to:
  - Hypovolemia
  - Decreased myocardial contractility
  - Anemia
- Decreased colloid osmotic pressure
- Edema
- Dysrhythmia
- Impaired temperature regulation
- Altered drug response
- Renal insufficiency
- Immunosuppression
- Infection/sepsis

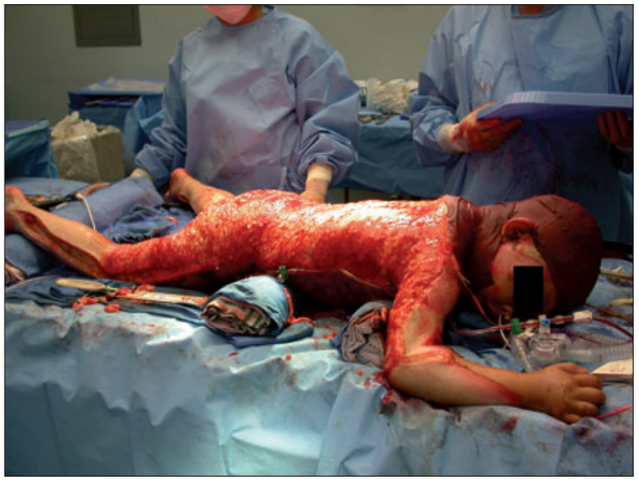


Fig. 14.1 As illustrated in this photograph anesthetic management of the acute burn patient for excision and grafting of wounds presents numerous challenges regarding monitoring, vascular access, temperature regulation, and rapid blood loss.

operative evaluation to assure that resuscitation has been optimized and an appropriate anesthetic plan has been formulated.

Preoperative evaluation

The preoperative evaluation of burn patients requires knowledge of the continuum of pathophysiological changes that occur in these patients from the initial period after injury through the time that all wounds have healed. The dramatic changes that occur in all organ systems following burn injury

TABLE 14.2 MAJOR PREOPERATIVE CONCERNS IN ACUTELY BURNED PATIENTS

Age of patient
Extent of burn injuries (total body surface area)
Burn depth and distribution (superficial or full thickness)
Mechanism of injury (flame, electrical, scald, or chemical)
Airway patency
Presence or absence of inhalation injury
Elapsed time from injury
Adequacy of resuscitation
Associated injuries
Coexisting diseases
Surgical plan

TABLE 14.3 FUNCTIONS OF SKIN

1. Protection from environmental elements (e.g. radiation, mechanical irritation or trauma)
2. Immunological — antigen presentation, antibacterial products (sebum), barrier to entry of pathological organisms
3. Fluid and electrolyte homeostasis — helps maintain protein and electrolyte concentrations by limiting evaporation
4. Thermoregulation — helps control heat loss through sweating and vasomotor regulation of superficial blood flow
5. Sensory — extensive and varied sensory organs in skin provide information about environment
6. Metabolic — vitamin D synthesis and excretion of certain substances
7. Social — appearance of skin has strong influence on image and social interactions
Adapted from Williams WG, Phillips LG. Pathophysiology of the burn wound. In: Herndon DN, ed. Total Burn Care, 1st edn. London: WB Saunders, 1996: 64.

directly affect anesthetic management. The following discussion will describe the pathophysiological changes that occur in the acutely burned patient as they relate to the preoperative evaluation. In addition to the routine features of the preoperative evaluation, evaluation of acute burn patients requires special attention to airway management and pulmonary support, vascular access, adequacy of resuscitation, and associated injuries. The severely burned patient presents with numerous preoperative concerns (Table 14.2).

The preoperative evaluation must be performed within the context of the planned operative procedure, which will depend on the location, extent, and depth of burn wounds, time after injury, presence of infection, and existence of suitable donor sites for autografting.

Initial evaluation of burn injury

Destruction of skin by thermal injury disrupts the vital functions of the largest organ in the body. The skin provides several essential protective and homeostatic functions (Table 14.3). Treatment of patients with burn injuries must compen-

sate for loss of these functions, until the wounds are covered and healed. As a barrier to evaporation of water, the skin helps maintain fluid and electrolyte balance. Heat loss through evaporation and impairment of vasomotor regulation in burned skin diminishes effective temperature regulation. The skin's barrier function also protects against infection by invading organisms. Wound exudate rich in protein depletes plasma proteins when large body surface areas are injured.

In addition to loss of important functions of the skin, extensive burns result in an inflammatory response with systemic effects that alter function in virtually all organ systems. Preoperative evaluation of the burn patient is guided largely by a knowledge of these pathophysiological changes.

Much of the morbidity and mortality associated with burn injuries are related to the size of the injury. The extent of the burn injury is expressed as the TBSA burned. Estimates of TBSA burned are used to guide fluid and electrolyte therapy and to estimate surgical blood loss. Percentage of the skin's surface that has been burned can be estimated by the so-called rule of nines (see Figure 14.2). Estimates are modified for pediatric patients because of age-related differences in body proportions. A knowledge of the burn depth is also critical to anticipating physiological insult, as well as, planned surgical treatment. First degree or superficial second degree burns may heal without scarring or deformity and do not require surgical excision. Deeper second degree and third degree burns require surgical debridement and grafting with associated surgical blood loss.

Accurate estimates of blood loss are crucial in planning preoperative management of burn patients. With extensive wound excision or debridement, large amounts of blood can be lost rapidly. Adequate preparation in terms of monitors, vascular access, and availability of blood products is essential. Surgical blood loss depends on area to be excised (cm^2), time since injury, surgical plan (tangential vs. fascial excision), and presence of infection.[10] Blood loss from skin graft donor sites will also vary depending on whether it is an initial or repeat harvest. These variables are valuable predictors of surgical blood loss, which is a critical factor in planning anesthetic management (Table 14.4).

Airway and pulmonary function

Special attention must be paid to the airway and pulmonary function during preoperative evaluation. Burn injuries to the face and neck can distort anatomy and reduce range of mobility in ways that make direct laryngoscopy difficult or impossible. Specific alterations include impaired mouth opening, edema of the tongue, oropharynx, and larynx, as well as decreased range of motion of the neck. The tissue injury and sloughing present after severe facial burns may make mask ventilation difficult. Inhalation injury may impair pulmonary gas exchange and lead to respiratory insufficiency or failure.

The level of respiratory support must also be assessed. The level of required support may range from supplemental blow-by or mask oxygen to intubation and ventilation with high positive end-expiratory pressure (PEEP) and FIO_2. Acute lung injury can occur from inhalation of chemical irritants, systemic inflammation from burn wounds or difficulties with resuscitation, or ventilator-induced injury. Common pathologies include upper thermal airway injury with stridor, pulmonary parenchyma damage from chemical irritants or inflammation, lower airway obstruction from mucus plugs and epithelial casts, as well as pulmonary edema due to acute lung injury or volume overload. With very high levels of PEEP or peak inspiratory pressure it must be determined if the anesthesia ventilator is adequate or if an ICU ventilator will need to be brought to the operating room. If the patient is intubated at the time of the preoperative evaluation it is essential to know what the indications for intubation were so that an appropriate plan for postoperative support can be made.

There is general recognition that smoke inhalation injury increases morbidity and mortality for burn patients.[11] The presence of an inhalation injury in combination with a cutaneous burn increases the volume of fluid required for resuscitation as much as 44%.[12] Numerous studies have also shown an increased incidence of pulmonary complications (pneumonia, respiratory failure, or ARDS) in patients with burns and inhalation injury when compared with burns alone.[13] Sequelae of inhalation injury include upper airway distortion and obstruction from direct thermal injury as well as impaired pulmonary gas exchange due to effects of irritant gases on lower airways and pulmonary parenchyma. These two components of the inhalation injury have separate time courses and pathophysiological consequences.

Foley described findings of 335 autopsies performed on patients who died from extensive burns.[14] Intraoral, palatal, and laryngeal burns were not uncommon among patients with inhalation injuries. The most common sites of laryngeal injury were the epiglottis and vocal folds where their edges were exposed. In contrast, thermal necrosis below the glottis and upper trachea was not observed in any of these patients. The lower airways are nearly always protected from direct thermal injury by the efficiency of heat exchange in the oro- and nasopharynx unless the injury involves steam or an explosive blast. This has been demonstrated in an experimental model.[15] Inhalation injury to the lower airways and pulmonary parenchyma is due to the effect of toxic or irritant gases.

Clinical suspicion of inhalation injury is aroused by the presence of certain risk factors such as history of exposure to fire and smoke in an enclosed space or a period of unconsciousness at the accident scene, burns including the face and neck, singed facial or nasal hair, altered voice, dysphagia, oral and/or nasal soot deposits, or carbonaceous sputum. The most immediate threat from inhalation injury is upper airway obstruction due to edema. Early or prophylactic intubation is recommended when this complication threatens. However, exposure to smoke does not always lead to severe injury and in the absence of overt evidence of respiratory distress or failure it may be difficult to identify patients who will experience progressive inflammation and ultimately require intubation of the trachea. In a retrospective study, Clark et al. reported that 51% of their patients exposed to smoke inhalation did not require intubation.[16] Unnecessary intubation in the presence of an inflamed laryngeal mucosa risks further damage to the larynx and subglottic area.[17,18]

Traditional clinical predictors of airway obstruction have been found to be relatively insensitive and inadequate for identifying early severe airway inflammation and often underestimate the severity of the injury.[19,20] More objective criteria for evaluation of the risk of airway obstruction are often

BURN DIAGRAM Shriners Burns Institute – Galveston Unit

Age: _____ Sex: _____ Date of admission: _____

Type of burn: Flame ☐ Electrical ☐ Scald ☐ Chemical ☐ Inhalation injury ☐

Date of burn _____

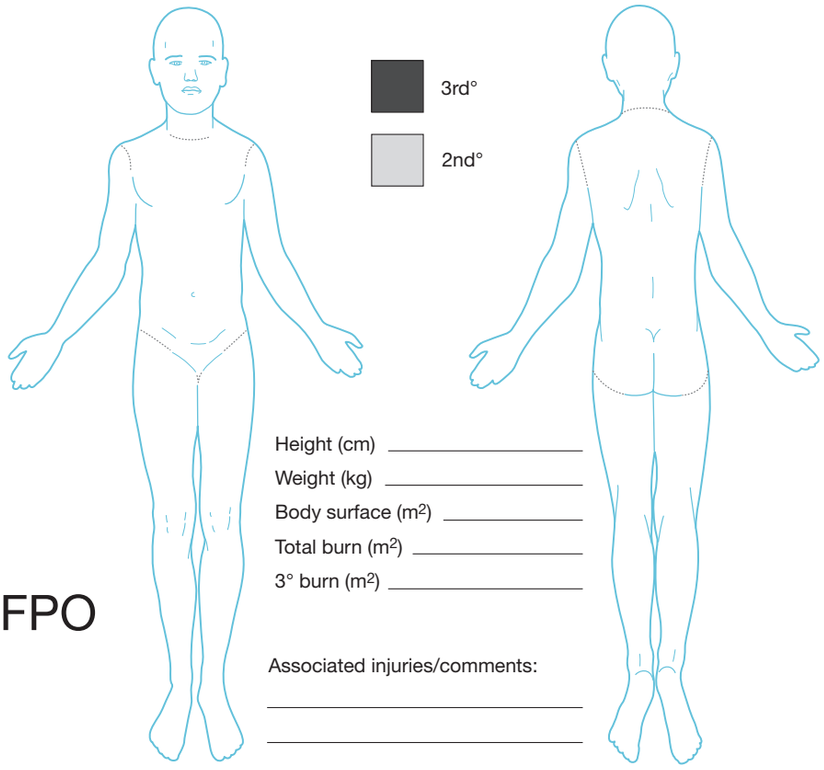
Date completed _____

Completed by _____

Date revised _____

Revised by _____

Approved by _____



Height (cm) _____

Weight (kg) _____

Body surface (m^2) _____

Total burn (m^2) _____

3° burn (m^2) _____

Associated injuries/comments:

_____

_____

Burn Estimate – Age vs. area

	Birth–1 year	1–4 years	5–9 1 year	10–14 years	15 years	Adult	2°	3°	TBSA%
Head	19	17	13	11	9	7			
Neck	2	2	2	2	2	2			
Anterior trunk	13	13	13	13	13	13			
Posterior trunk	13	13	13	13	13	13			
Right buttock	2.5	2.5	2.5	2.5	2.5	2.5			
Left buttock	2.5	2.5	2.5	2.5	2.5	2.5			
Genitalia	1	1	1	1	1	1			
Right upper arm	4	4	4	4	4	4			
Left upper arm	4	4	4	4	4	4			
Right lower arm	3	3	3	3	3	3			
Left lower arm	3	3	3	3	3	3			
Right hand	2.5	2.5	2.5	2.5	2.5	2.5			
Left hand	2.5	2.5	2.5	2.5	2.5	2.5			
Right thigh	5.5	6.5	8	8.5	9	9.5			
Left thigh	5.5	6.5	8	8.5	9	9.5			
Right leg	5	5	5.5	6	6.5	7			
Left leg	5	5	5.5	6	6.5	7			
Right foot	3.5	3.5	3.5	3.5	3.5	3.5			
Left foot	3.5	3.5	3.5	3.5	3.5	3.5			
						Total			

Fig. 14.2 Modified from Lund and Browder. Chart used to calculate the surface area involved by burn. It takes into account that, as one grows from infancy to adulthood, the relative surface area of the head decreases while the relative surface area of the lower extremities increases.

TABLE 14.4 CALCULATION OF EXPECTED BLOOD LOSS

Surgical procedure	Predicted blood loss
<24 h since burn injury	0.45 mL/cm^2 burn area
1–3 days since burn injury	0.65 mL/cm^2 burn area
2–16 days since burn injury	0.75 mL/cm^2 burn area
>16 days since burn injury	0.5–0.75 mL/cm^2 burn area
Infected wounds	1–1.25 mL/cm^2 burn area

Adapted from Desai et al., Ann Surg 1990.[7]

needed. Hunt et al. found fiberoptic bronchoscopy to be a safe and accurate method for diagnosis of acute inhalation injury.[21] They described observations of severe supraglottic injuries associated with mucosal edema obliterating the piriform sinuses and causing massive enlargement of the epiglottis and arytenoid eminence. Haponic et al. made serial observations by nasopharyngoscopy in patients at risk for inhalation injury and found distortions of the upper airway described as compliant, edematous mucosa of the aryepiglottic folds, and arytenoid eminences that prolapsed to occlude the airway on inspiration.[22] Progressive upper airway edema in these patients was correlated with body surface area burned, resuscitative volume administered, and rate of infusion of resuscitative fluids. For patients who are at risk for inhalation injury but lack definitive indications for intubation, fiberoptic nasopharyngoscopy is effective in identifying laryngeal edema. Serial exams may help avoid unnecessary intubations and at the same time identify progressive inflammatory changes and allow intubation before severe airway obstruction and emergent conditions develop.

Lower airway and parenchymal injuries develop more slowly than upper airway obstruction. Prior to resuscitation, clinical signs and symptoms, chest x-ray, and blood gas analysis may be within normal limits despite significant injury that eventually progresses to respiratory failure requiring intubation and mechanical ventilation.[23]

Linares et al. studied the sequence of morphological changes following smoke inhalation in an experimental sheep model.[24] They observed four discrete but overlapping phases of injury described as exudative, degenerative, proliferative, and reparative. During the first 48 hours the *exudative phase* was characterized by polymorphonuclear (PMN) infiltration, interstitial edema, loss of Type I pneumocytes, and damage to the tracheobronchial epithelium in the form of focal necrosis, hemorrhage, and submucosal edema. The *degenerative phase* occurred between 12 and 72 hours and was characterized by progressive epithelial damage with shedding of necrotic tissue and formation of pseudomembranes and casts. Hyaline membranes developed over alveolar surfaces. Macrophages began to accumulate to begin absorption of necrotic debris. A *proliferative phase* was described between days 2 and 7 during which Type II pneumocytes and macrophages proliferated. After the fourth day *reparative* changes were observed with regeneration of epithelium from spared epithelium from the orifices of glands.

Demling and Chen have provided a lucid description of the pathophysiological changes following inhalation injury.[25] Decreased dynamic compliance increases the work of breathing. Increased closing volume and decreased functional residual capacity lead to atelectasis and shunt resulting in hypoxia. Airways become plugged by sloughed epithelium, casts, and mucus. Impaired ciliary action exacerbates the airway obstruction by decreasing the clearance of airway debris. These changes lead to further shunt and allow colonization and pneumonia. Treatment for inhalation injury is empiric and supportive with tracheal intubation and mechanical ventilation. The application of aggressive pulmonary toilet, high-frequency percussive ventilation, and respiratory therapy protocols designed to mobilize obstructing debris are also highly beneficial. The importance of strategies to limit ventilator-induced lung injury has been recognized.[26–30]

Carbon monoxide (CO) and cyanide are two major toxic components of smoke. The burn patient with evidence of inhalation injury should be evaluated for the presence of toxicity resulting from these compounds. CO binds hemoglobin 200 times more avidly than oxygen.[31] Therefore, CO markedly impairs the association of oxygen with hemoglobin and decreases oxygen-carrying capacity. CO also shifts the oxyhemoglobin dissociation curve to the left, thus decreasing the release of oxygen into tissues. These factors result in decreased oxygen delivery to tissues and, at critical levels, lead to anaerobic metabolism and metabolic acidosis. Signs and symptoms of CO poisoning include headache, mental status changes, dyspnea, nausea, weakness, and tachycardia. Patients suffering CO poisoning have a normal PaO_2 and oxygen saturation by routine pulse oximetry. They are not cyanotic. Carboxyhemoglobin must be detected by co-oximetry. Carboxyhemoglobin levels above 15% are toxic and those above 50% are often lethal. The major treatment approach is administration of 100% oxygen and, in severe cases, hyperbaric treatment to increase the partial pressure of oxygen in blood.[32]

Cyanide is also a component of smoke, resulting from the burning of certain plastic products.[33] Cyanide directly impairs the oxidative apparatus in mitochondria and decreases the ability of cells to utilize oxygen in metabolism. These alterations result in conversion to anaerobic metabolism and the development of metabolic acidosis. Signs and symptoms include headache, mental status changes, nausea, lethargy, and weakness. Hydrogen cyanide levels above 100 ppm are generally fatal.[34,35]

Treatment of cyanide toxicity begins with a high inspired oxygen concentration, which may increase intracellular oxygen tension enough to cause non-enzymatic oxidation of reduced cytochromes, or displace cytochrome oxidase and potentiate the effects of administered antidotes. Pharmacological intervention includes methemoglobin generators such as the nitrates (amyl nitrite inhalation 0.2 mLs, or sodium nitrite intravenous 10 mL of 3% solution for adults and 0.13–0.33 mL/kg of 3% solution for pediatrics) and dimethylaminophenol (3.25 mg/kg) to increase methemoglobin levels. Methemoglobin competes with cytochrome oxidase for cyanide. However, excessive levels of methemoglobin lead to decreased oxygen-carrying capacity and may be toxic. Direct binding agents have a high affinity for cyanide. Di-cobalt edetate (20 mL of 15% solution for adults or 0.3–0.5 mL/kg of 15% solution for pediatrics) is

extremely rapid in action but has significant toxicity; where hydroxocobalamin (adults 5–10 g or pediatrics 70 mg/kg) the precursor of vitamin B_{12} has been shown to be safe with few systemic side effects, is actively metabolized by the liver and avoids renal absorption. Sulphur donors such as sodium thiosulphate (adults 25 mL of 50% solution or pediatrics 1.65 mL/kg of 25 % solution) accentuate the bodies' enzymatic conversion of cyanide to thiocyanate in the presence of the mitochondrial enzyme rhodanese decreasing its toxicity and increasing elimination.[34,35]

Effect of burn injury on circulation

Thermal injury has profound effects on the systemic circulation, and hemodynamic management is a major component of perioperative care. It is critical for the anesthesiologist to assess the adequacy of postburn fluid resuscitation and the hemodynamic status of the patient. Important variables include blood pressure, heart rate, urine output, central venous pressure, base deficit, and blood lactate levels. In patients with pulmonary artery catheters, cardiac output, mixed venous oxygen saturation, cardiac and pulmonary filling pressures, and oxygen delivery parameters provide important information regarding the hemodynamic status of the burn patient. In addition, determination of blood hemoglobin level, fluid requirements, and the need for pressors or inotropes are important for developing an effective anesthetic plan.

After massive thermal injury, a state of burn shock develops due to intravascular hypovolemia and, in some cases, myocardial depression. This state of burn shock is characterized by decreased cardiac output, increased systemic vascular resistance, and tissue hypoperfusion.[36,37] Intravascular hypovolemia results from alterations in the microcirculation in both burned and unburned tissues, leading to the development of massive interstitial fluid accumulation. Cutaneous lymph flow increases dramatically in the immediate postburn period and remains elevated for approximately 48 hours.[38] The forces responsible for this massive fluid shift involve all components of the Starling equilibrium[39]

$$J_v = K_f\,[(P_c - P_{if}) - s(?_p - ?_i)] \text{ where:}$$

K_f is the capillary filtration coefficient, P_c is the capillary pressure, P_{if} is the interstitial hydrostatic pressure, s is the reflection coefficient for protein, $?_p$ is the plasma colloid osmotic pressure and $?_{if}$ the interstitial colloid osmotic pressure.

The specific alterations include:

- an increased microvascular permeability coefficient (k_f and s) due primarily to the release of local and systemic inflammatory mediators;
- an increase in intravascular hydrostatic pressure (P_c) due to microvascular dilatation;
- decreased interstitial hydrostatic pressure (P_i);
- decreased intravascular oncotic pressure (π_c) due to leakage of protein from the intravascular space; and
- a relative increase in interstitial oncotic pressure due to a smaller decrease in interstitial oncotic pressure (π_i) compared to intravascular oncotic pressure (π_c).

The leakage of protein and fluid into the interstitial space often results in a washout of the interstitium and markedly increased lymph flow. The net effect of these changes is the development of massive edema during the first 24–48 hours after thermal injury with a concomitant loss of intravascular volume. The hypotension associated with burn injury is also due, in part, to myocardial depression. The inflammatory response to thermal injury results in the release of large amounts of inflammatory mediators such as tumor necrosis factor α (TNFα), interleukin-1 (IL-1), and prostaglandins. TNFα and IL-1 are known to have myocardial suppressant effects.[45,46] These factors, and other possibly unrecognized factors, are responsible for the depression in myocardial function that often results from burn injury.

If the patient survives the initial burn shock and is adequately resuscitated, a state of hyperdynamic circulation develops that is mediated by a variety of inflammatory mediators. This state of massive inflammation has been termed the systemic inflammatory response syndrome (SIRS) and is characterized by hypotension, tachycardia, a marked decrease in systemic vascular resistance, and increased cardiac output. SIRS has a continuum of severity ranging from the presence of tachycardia, tachypnea, fever, and leukocytosis to refractory hypotension and, in its most severe form, shock and multiple organ system dysfunction. In thermally injured patients, the most common cause of SIRS is the burn itself; however, sepsis, SIRS with the presence of infection or bacteremia, is also a common occurrence.

Burn patients require large volume fluid resuscitation in the immediate postburn period. This is due to a state of burn shock that develops in the immediate postburn period as described earlier. Several resuscitation protocols that utilize various combinations of crystalloids, colloids, and hypertonic fluids have been developed (Table 14.5). Isotonic crystalloid resuscitation is the most commonly used fluid for initial resuscitation in US burn centers. The most popular fluid resuscitation regimen, the Parkland Formula, uses isotonic crystalloid solutions and estimates the fluid requirements in the first 24 hours to be 4 mL/kg/% TBSA, although, many burn centers are administering 50% more fluid than the Parkland Formula would predict.[47] Crystalloid solutions generally provide adequate volume resuscitation, however, the large volumes that are needed result in substantial tissue edema and hypoproteinemia. Therefore, interest has developed in analyzing colloid and hypertonic resuscitation regimens. Overall, colloid resuscitation within the first 24 hours of burn injury has not improved outcome compared to crystalloid resusciation.[48,49] Furthermore, a recent meta-analysis indicated that mortality is higher in burned patients receiving albumin as part of the initial resuscitation protocol with a 2.4 relative risk of mortality compared to patients receiving crystalloid alone.[50] Because of the added cost with little established benefit, colloid solutions have not been used routinely in the United States for initial volume resuscitation in burned patients. Recently, however, in a prospective, randomized study use of plasma for volume resuscitation has been found to limit volume infused along with intra-abdominal pressure and abdominal compartment syndrome (see below).[51] These outcome variables have not been used for comparing crystalloid and colloid resuscitation in the past. With the trend toward larger volumes for initial resuscitation it may be that the use of colloid may be beneficial for larger injuries requiring more volume.

TABLE 14.5 FORMULAS FOR ESTIMATING ADULT BURN PATIENT RESUSCITATION FLUID NEEDS

Colloid formulas	Electrolyte	Colloid	D5W
Evans	Normal saline 1.0 mL/kg/% burn	1.0 mL/kg/% burn	2000 mL/24 h
Brooke	Lactated Ringer's 1.5 mL/kg/% burn	0.5 mL/kg	2000 mL/24 h
Slater	Lactated Ringer's 2 liter/24 h	Fresh frozen plasma	75 mL/kg/24 h
Crystalloid formulas			
Parkland	Lactated Ringer's	4 mL/kg/% burn	
Modified Brooke	Lactated Ringer's	2 mL/kg/% burn	
Hypertonic saline formulas			
Hypertonic saline solution (Monafo)	Volume to maintain urine output at 30 mL/h Fluid contains 250 mEq Na/liter		
Modified hypertonic (Warden)	Lactated Ringer's +50 mEq NaHCO3 (180 mEq Na/liter) for 8 hours to maintain urine output At 30–50 mL/h Lactated Ringer's to maintain urine output at 30–50 mL/h beginning 8 hours postburn		
Dextran formula (Demling)	Dextran 40 in saline — 2 mL/kg/h for 8 hours Lactated Ringer's — volume to maintain urine output at 30 mL/h Fresh frozen plasma — 0.5 mL/kg/h for 18 hours beginning 8 hours postburn		

The use of hypertonic saline, either alone or in conjunction with colloids, has also been advocated by some in the initial resuscitation of burned patients. Among the potential benefits are reduced volume requirements to attain similar levels of intravascular resuscitation and tissue perfusion compared to isotonic fluids.[52] Theoretically, the reduced volume requirements would decrease the incidence of pulmonary and peripheral edema, thus reducing the incidence of pulmonary complications and the need for escharotomy. Hypertonic saline dextran solutions have been shown to expand intravascular volume by mobilizing fluids from intracellular and interstitial fluid compartments. Although hypertonic saline dextran solutions will transiently decrease fluid requirements, there is a potential for a rebound in fluid resuscitation needs.[53,54] Therefore, most burn centers continue to employ isotonic crystalloid fluids for initial resuscitation of patients in burn shock.

Several parameters have been used to assess the adequacy of volume resuscitation in burned patients (Table 14.6). Unfortunately there is no single physiological variable that is always reliable as an end point to guide resuscitation in acute burn patients. The overall goal is early volume resuscitation and establishment of tissue perfusion. Traditionally, urine output (0.5–1 mL/kg/h) and normalization of blood pressure (mean arterial blood pressure of greater than 70 mmHg) have been used as endpoints. However, recent studies indicate that these parameters may be poor predictors of adequate tissue perfusion. Jeng and colleagues showed that attaining urine outputs of greater than 30 mL/h and mean blood pressures of greater than 70 mmHg correlated poorly with other global indicators of tissue perfusion such as base deficit and blood lactate levels.[55] In order to maintain perfusion of vital organs such as heart and brain, blood flow is often redistributed away from splanchnic organs. Persistent hypoperfusion of these organs ultimately results in tissue injury and may be a contributing factor to multisystem organ dysfunction. Several studies have shown that normalization of blood pressure, heart rate, and urine output do not correlate with improved outcome.[56,57] Therefore, in the preoperative assessment of the burn patient, the anesthesiologist should not base the cardiovascular assessment strictly on these parameters.

TABLE 14.6 CRITERIA FOR ADEQUATE FLUID RESUSCITATION

- Normalization of blood pressure
- Urine output (1–2 mL/kg/h)
- Blood lactate (<2 mmol/liter)
- Base deficit (<–5)
- Gastric intramucosal pH (>7.32)
- Central venous pressure
- Cardiac index (CI) (4.5 liter/min/m^2)
- Oxygen delivery index (DO_2I) (600 mL/min/m^2)

Invasive cardiovascular monitors are not used routinely in burned patients to guide volume resuscitation. Most patients can be adequately resuscitated without their use. However, a small subset of patients, such as those with underlying cardiovascular disease or those who do not respond normally to volume resuscitation, may benefit from invasive monitoring. Some investigations have focused on the use of cardiac index and oxygen delivery as useful endpoints to guide volume resuscitation.[58,59] One way in which shock can be defined is oxygen debt. Therefore, maintaining an adequate cardiac index and oxygen delivery capacity such that oxygen delivery meets oxygen consumption provide useful criteria in guiding volume resuscitation. Bernard and colleagues have shown that patients surviving large burn injuries had higher cardiac indices and more effective oxygen delivery than nonsurvivors.[60] Some investigators have proposed the use of supranormal oxygen delivery as a means of assuring adequate tissue

perfusion.[61,62] The preselected goals were a cardiac index of 4.5 1/m^2 and an oxygen delivery index of 600 mL/min/m^2. These values represent approximately 150% of normal cardiac index and oxygen delivery values. Attaining supraphysiological cardiac output and oxygen delivery has been shown to improve outcome in some studies. Schiller and colleagues demonstrated that maintaining a hyperdynamic hemodynamic state using fluids and inotropes improved survival in burn patients.[63] However, other investigations, including a meta-analysis, have shown that achieving supra-physiological levels of cardiac output and oxygen delivery did not improve mortality or decrease the incidence of organ failure in trauma and burn patients.[64–66] The use of inotropes to attain supra-physiological oxygen transport could be detrimental in some cases. One study that employed dobutamine to increase cardiac output and increase oxygen delivery demonstrated increased mortality.[67]

Estimating preload in the acutely burned patient is quite challenging. Filling pressures (central venous pressure and pulmonary artery occlusion pressure) correlate poorly with circulating blood volume especially during positive pressure ventilation.[68] A single indicator transcardiopulmonary thermodilution technique has been used to estimate the volume of blood in the thorax (intrathoracic blood volume or ITBV).[69] This technique has been used in burn patients during resuscitation. Holm and colleagues observed that where neither central venous pressure nor pulmonary capillary wedge pressures correlated with changes in cardiac index or oxygen delivery during fluid resuscitation of burn patients, there was a moderate correlation of these variables with ITBV.[70] This monitor was used successfully to resuscitate 24 severely burned patients. Volumes administered were significantly larger than predicted by the Parkland formula.[70] This technology is available commercially as the PiCCO system (Pulsion Medical Systems, Munich, Germany). In addition to ITBV this system also provides an estimate of extravascular lung water and continuous estimate of cardiac output and systemic vascular resistance.

Blood lactate and base deficit provide indirect metabolic global indices of tissue perfusion. Lactic acid is a byproduct of anaerobic metabolism and is an indicator of either inadequate oxygen delivery or impaired oxygen utilization. In the absence of conditions such as cyanide poisoning or sepsis that alter oxygen utilization at the cellular level, lactate production serves as a useful marker of oxygen availability. Serum lactate levels have served as a useful marker of fluid resuscitation and tissue perfusion in burn patients.[71] A recent study showed serum lactate to be the most predictive index of adequate tissue perfusion and a lactate level of less than 2 mmol/L in the first 24–72 hours after burn injury correlated with increased survival.[57] Base deficit is another indirect indicator of global tissue perfusion. The base deficit is calculated from the arterial blood gas using the Astrup and Siggard-Anderson nomograms. Although it is not directly measured, base deficit provides a readily obtained and widely available indicator of tissue acidosis and shock. Base deficit has been shown to correlate closely with blood lactate and provides a useful indicator of inadequate oxygen delivery. A retrospective study by Kaups et al. showed that base deficit was an accurate predictor of fluid requirements, burn size, and mortality rate.[73]

Lactate and base deficit serve as global markers of tissue perfusion and oxygen delivery. However, in burn patients, tissue perfusion is not uniform. Perfusion of the splanchnic beds is often sacrificed in order to maintain the perfusion of heart, brain, and kidneys. The use of gastric intramucosal pH (pH_i) has been advocated as a measure of splanchnic perfusion. Several studies have shown that measurement of pH_i is useful in guiding resuscitation and that low pH_i is a predictor of organ failure and death.[74] pH_i is measured by gastric tonometry and can provide useful information regarding tissue perfusion.

Formulae for resuscitation of burns provide an approximation of fluid needs but volumes actually administered need to be individualized for each patient. Although two patients may each have 50% TBSA burns, it is not likely that their wounds will be equivalent otherwise. Several factors can increase fluid requirements (Table 14.7). Deep full thickness burns require larger volume than partial thickness injuries. Likewise, extensive soft tissue damage from electrical burns or crush injuries increase fluid needs. Inhalation injury can also increase fluid requirements as much as 50% as noted above.[12] These differences in wounds and fluid requirements among patients makes it very difficult at times to optimize fluid administration. None of the physiological end points is always reliable. All available clinical information must be examined and each variable evaluated within the context of all the other variables.

It has been observed that over the past several years that increased volumes of crystalloid solutions are being used for resuscitation of burn patients.[75] In many cases as much as twice the volume recommended by the Parkland formula is used. As a consequence, patients experience increased edema. During the preoperative evaluation attention must be paid to the degree to which edema produces physiologic derangements. The edema can lead to compartment syndrome of extremities or abdomen (Figure 14.3). Blindness due to ischemic optic neuropathy has been reported as a complication of burn resuscitation.[76] Increased intra-abdominal pressure is a complication of vigorous fluid resuscitation which may be more common than generally appreciated and may often explain difficulties with resuscitation. Greenhalgh and Warden first described the association of increased abdominal pressures and compartment syndrome with burn resuscitation.[77] Ivey and colleagues prospectively studied 10 adult patients presenting with greater than 20% TBSA burns and found that 70% of these patients had at least transient intra-abdominal hypertension.[78] Two of their patients with more than 80% TBSA burns developed

TABLE 14.7 FACTORS THAT MAY INCREASE FLUID NEEDS FOR RESUSCITATION OF PATIENTS WITH ACUTE BURN INJURIES

• Inhalation injury
• Delay in resuscitation
• Crush injury
• Electrical injury
• Large full thickness burns
• Methamphetamine lab accidents
• Associated injuries

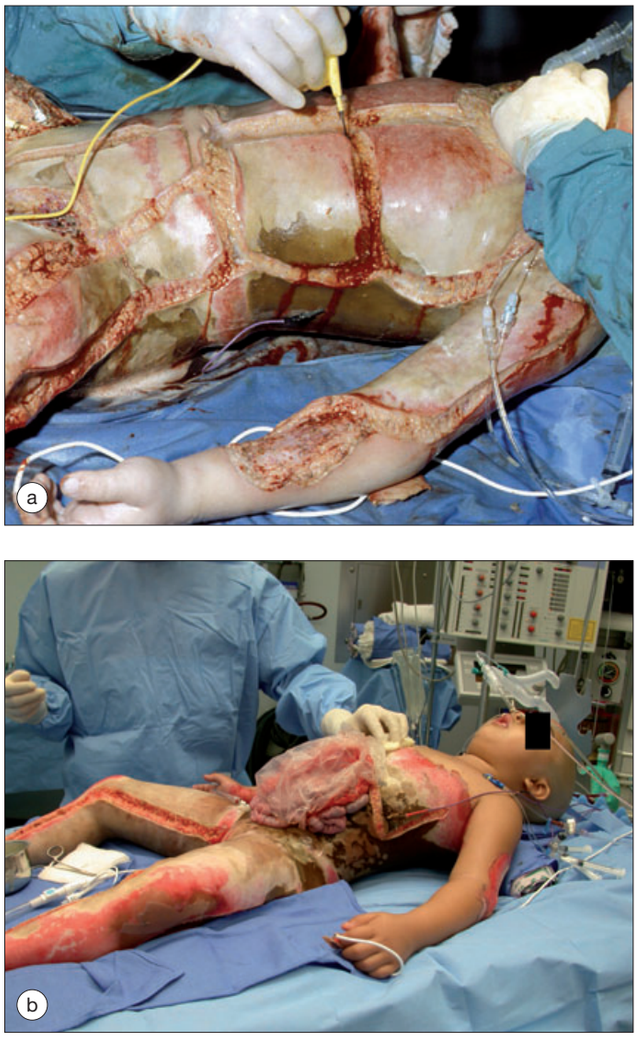


Fig. 14.3 Large volumes of crystalloid solution required for resuscitation of patients with acute burns can be associated with compartment syndrome of extremities and abdomen. (a) Escarotomies can decompress these compartments but (b) laparotomy may be required for abdominal compartment syndrome when escarotomies do not adequately decompress the abdomen.

abdominal compartment syndrome requiring surgical decompression. Several studies since then have described the common occurrence of increased intra-abdominal pressure with large volume burn resuscitation. Increased intra-abdominal hypertension is termed abdominal compartment syndrome when it is associated with impaired respiration, circulation, and urine output. Mechanical ventilation is impaired by pressure on the diaphragm, circulation is impaired by restricted venous return due to caval compression, and urine output is impaired by compression of renal vessels. When this pattern presents the patient should be examined for elevated intra-abdominal pressure. This can be accomplished by measuring bladder pressure: 50 mL of saline is instilled into the bladder through the Foley catheter and the height of the saline column above the symphysis pubis is measured (1.36 cm of H_2O = 1 mmHg).[79]

Conservative treatment of elevated intra-abdominal pressure includes attempts to limit the volume of intravenous fluid needed for resuscitation. The inclusion of plasma with infused fluids has been found to reduce volume required and was associated with significantly lower intra-abdominal pressures.[51] In addition adequate analgesia and sedation should be achieved. Diuresis with furosemide and muscle relaxants to reduce muscle tone have been used to reduce intra-abdominal pressure. More invasive measures include escharotomies,[80] percutaneous peritoneal dialysis catheter drainage,[81] and laparotomy.[77]

Recently several clinicians have reported a specific type of burn injury that has been associated with difficulties with resuscitation.[82–84] There has been a dramatic increase in burn injuries from explosions and fires related to methamphetamine production in illicit labs. Victims of these accidents present unique challenges for a variety of reasons. Substances used in methamphetamine production include chemicals that are corrosive and toxic (eg. anhydrous ammonia, hydrochloric acid, red phosphorous, and ephedrine). Other ingredients are flammable (acetone, alcohol, and gasoline) and explosions can coat the victims with all these chemicals. As a result, in addition to the victim's toxic exposure, contacting incompletely decontaminated victims of these accidents has injured first responders and hospital workers.[85,86]

In addition to exposures described above, these patients are usually intoxicated with methamphetamine, as demonstrated by positive urine screen, and may have inhaled toxic fumes such as phosphine gas. Santos et al. found the incidence of inhalation injury twice as great in victims of methamphetamine-related burns as in age and burn-matched controls.[82] Among their patients requiring intubation for inhalation injury methamphetamine users also required roughly twice as many ventilator days.

Clinical studies have consistently observed increased fluid requirements for resuscitation of methamphetamine patients.[82,85] For example, Santos et al. found that resuscitation volumes were 1.8 times greater for methamphetamine users with burns than controls.[82]

Methamphetamine users with burns experienced more behavioral problems also. These patients are more often agitated and require restraints. Santos et al. reported that all their methamphetamine patients required greater than normal doses of sedatives and displayed what they referred to as 'withdrawal type syndrome.' [82] This behavior may be due to withdrawal of methamphetamine from chronic users.

Effect of burn injury on renal function

Acute renal failure (ARF) is a relatively common complication following major burn injuries. The incidence of ARF following burn injury has been reported to range from 0.5 to 30% and is most dependent on the severity of the burn and the presence of inhalation injury.[87–89] The development of ARF is a poor prognostic indicator with mortality rates as high as 100% reported by some investigators.[90] However, Jeschke and colleagues have shown a decrease in mortality in pediatric burn patients with ARF to 56% since 1984.[91] Holm and colleagues observed that ARF could be divided into early and late categories. Early ARF was defined as occurring within 5 days of burn

injury.[92] The most common apparent causes were hypotension and myoglobinuria. ARF occurring after 5 days of injury was defined as late. Here, sepsis was the most common cause with a small number of cases resulting from the administration of nephrotoxic drugs. Factors that will decrease the incidence of ARF and, if it occurs, associated mortality include adequate fluid resuscitation, early wound excision, and prevention of infection.[93] Regardless of the cause, it is critical to assess renal function in burn patients in order to develop a comprehensive anesthetic plan. Important areas of analysis include urine output, dialysis dependence, volume status, and electrolytes; also diuretic therapy should be noted. Scheduled doses of diuretics may need to be continued during the perioperative period to maintain urine output.

Metabolic changes associated with burn injury

Increased metabolic rate is the hallmark of the metabolic alteration that takes place after thermal injury. The magnitude of the hypermetabolism is influenced by the size of the burn wound, how the burn patient is treated and the ambient temperature of the patient.[94,95]. Within the range of 30–70% TBSA burn injury the hypermetabolism tends to be proportionate to the size of the burn wound. With burns beyond this range the hypermetabolism appears to plateau and only increases in smaller increments.[96] Septic complication is an important factor that can increase the metabolic response and so does the physiologic stress of pain. It has been observed that modern day treatment of burn injuries with early excision and closed wound treatment ameliorates the hypermetabolism.[97] As mentioned earlier burn patients increases their metabolic rate in an effort to generate heat according to a new threshold set point for the body temperature that is influenced by the size of the burn (see below: Thermoregulation in burn patients). The recognition of this fact has lead to an increased awareness of the importance of the ambient temperature in modulating the hypermetabolism of the burn patient. Using indirect calorimetry in acute patients with major burn injuries that are treated according to current standards resting energy expenditures that are 110–150% above predicted values are frequently measured.[98]

As a result of the hypermetabolic response the burned patient has an increased O_2 consumption along with an increased CO_2 production that collectively demands a higher respiratory effort. The anesthetic care of the acute burned patient has to accommodate these changes and frequently this has to be done in patients with compromised pulmonary function due to burn injury.

According to the hypermetabolism the caloric needs of the burn patient are also increased. Further more, numerous studies have shown that optimized nutritional care not only can ameliorate the burn associated state of catabolism and immune suppression but also improves wound healing.[94] Oral or enteral feeding is recognized as the optimal feeding route of the burned patient. Frequently the acute burn patient has to be fed continuously over extended time periods. This is not only because of the increased caloric needs but also because of compromised gastric emptying and decreased intestinal motility that necessitates a slower feeding rate of critically ill patients. If standard guidelines for perioperative fasting are implemented recurrent operative procedures can significantly impinge on the nutritional needs of the patient and ultimately cause a caloric deficit. To accommodate the nutritional needs of the patient a continuation of duodenal nutrition perioperatively has been advocated. Studies indicate that not only is this procedure safe but it might also provide for a favorable gut oxygen balance.[99]

At the time of the withdrawal of ventilator support and extubation the metabolic state of the burn patient should be considered. The characteristic catabolic state of major burn injury spares no muscles[100] and the respiratory muscles are affected. Along with decreased muscle strength there is frequently decreased pulmonary compliance not only due to the formation of scar tissue and pulmonary interstitial changes but also due to increased intra-abdominal content. Burn associated hepatomegaly along with gastrointestinal retention can significantly impinge on respiratory reserves.[101]

Severe insulin resistance with hyperglycemia and concurrent hyperinsulinemia is a key feature of the metabolic alterations of burn injury.[95] It is well recognized that critically ill patients with insulin resistance benefit from tight glycemic control in the ICU[102] and these findings have been expanded to the burn patient population.[103] During the intraoperative period the question is less studied. Although the benefit of tight intraoperative glycemic control has been documented in other patient populations,[104] the risk versus benefit during anesthesia has not been studied specifically in burn patients.

Thermoregulation in burn patients

Maintenance of proper body temperature is an important factor in the care of severely burned patients. The thermoregulatory system is controlled by three major components. These include the afferent system that senses changes in core body temperature and transmits this information to the brain, the central regulatory mechanisms located primarily in the hypothalamus that process afferent input and initiate responses, and the efferent limb that mediates specific biological and behavioral responses to changes in core body temperature (Figure 14.4). Temperature is sensed by Aδ and C fibers present in peripheral tissues such as skin and muscle as well as core tissues such as brain, deep abdominal tissues, and thoracic viscera.[105] The vast majority of afferent input arises from the core tissues. Because the skin is in direct contact with the environment, it senses immediate changes in environmental temperature. However, the overall afferent input of the skin and other peripheral tissues is estimated to be only 5–20% of total afferent thermoregulatory input.[105] Therefore, loss of skin following a burn injury is not likely to markedly alter overall afferent input. Wallace and colleagues have shown that burn patients perceive changes in ambient temperature as effectively as normal controls.[106] This is likely due to the retained ability of burn patients to sense changes in core temperature and transmit this information to the central nervous system. Central control of temperature is a complicated system that is not well understood. The hypothalamus plays an important role in temperature regulation, but the complete mechanism of temperature control is likely to be multifaceted and is an area of intense research. Regard-

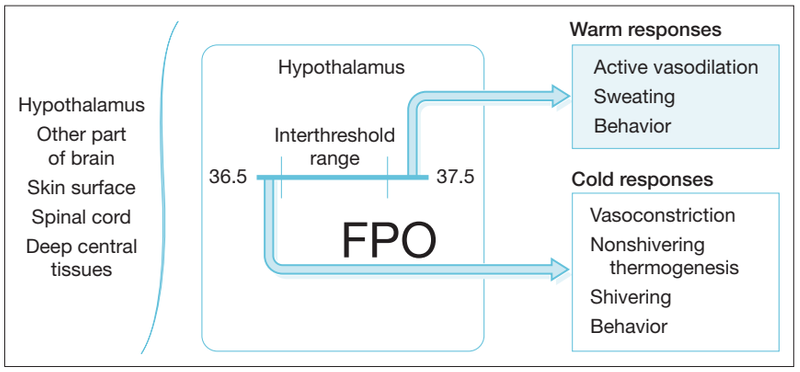


Fig. 14.4 Schematic demonstrating thermoregulatory control mechanisms. Afferent input from a variety of sites, most notably skin, central tissues and brain, are processed in the central nervous system. Based on input, a variety of efferent thermoregulatory responses are initiated. (From: Sessler DI. Temperature monitoring. In: Miller R, ed. Anesthesia 3rd edn. New York: Churchill Livingstone; 1990.)

less of the ultimate control mechanisms, temperature control can be divided into three main functions: threshold, gain, and maximum response intensity.

Threshold encompasses a set point at which responses to temperature change are initiated. In normal individuals the threshold range is generally near 36.5–37.5°C. In burn patients, the threshold set point is higher and the increase is proportional to the size of the burn. The work of Caldwell and colleagues predicts that the temperature set point will increase by 0.03°C% TBSA burn.[107] This increase in temperature threshold appears to be due to the hypermetabolic state and the presence of pyrogenic inflammatory mediators such as TNF, IL-1, and IL-6 that are present after thermal injury. The elevated temperature set point can be decreased by administration of indomethacin, which suggests prostaglandins act as final common mediators of this response.[108,109]

Gain describes the intensity of response to alterations in temperature. In most cases the gain of thermoregulatory responses is very high with response intensity increasing from 10 to 90% with only a few tenths of a degree change in core temperature. This response is maintained in most burn patients, resulting in a further increase in metabolic rate.[106] Burn patients respond with a brisk increase in heat generation and metabolic rate in response to changes in core body temperature.[106] However, work by Shiozaki and colleagues has shown that burn patients who are slow to respond to postoperative hypothermia are at increased risk of mortality.[110] The decreased responsiveness may be due, in part, to tissue catabolism, poor nutrition, or sepsis. In addition, the response to relative hypothermia is characterized by increased catecholamine release, tissue catabolism, and hypermetabolism. These responses further stress burn patients, and decrease their ability to respond to their primary injury.[111]

The most important efferent responses to hypothermia are behavioral responses such as gaining shelter, covering up and seeking a more desirable ambient temperature. In the acute post burn setting, most of these behaviors are impeded by positioning, sedation and inability to seek a more favorable environment. Therefore, caregivers must be attentive to the patient's temperature and perception of cold so that measures can be undertaken to optimize the patient's temperature. Cutaneous vasoconstriction is another important mechanism for preserving heat and core body temperature. In unburned persons, a temperature gradient of 2–4°C exists between skin and core tissues. This gradient is maintained by cutaneous vasoconstriction. Without cutaneous vasoconstriction, heat is

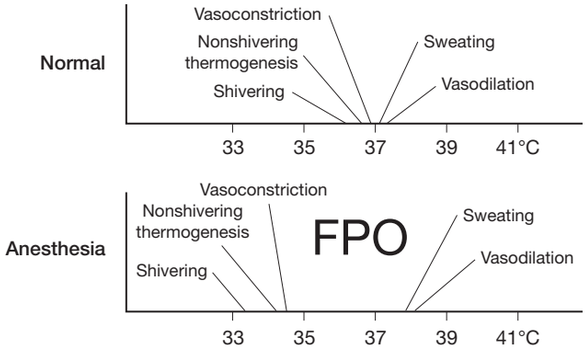


Fig. 14.5 Effects of anesthesia on thermoregulatory mechanisms. (From: Sessler DI. Temperature monitoring. In: Miller R, ed. Anesthesia. 3rd edn. New York: Churchill Livingstone; 1990.)

redistributed from the core compartment to the periphery. This heat is ultimately lost to the environment. Peripheral vasoconstriction minimizes temperature redistribution and acts to maintain core body temperature. This mechanism of heat preservation is lost with the loss of large areas of skin, particularly if cutaneous tissues are excised down to the fascial level. The loss of skin facilitates the loss of core body heat into the environment and places the burn patient at risk for core hypothermia. Another mechanism of heat loss in burn patients is evaporation. Burn patients can lose as much as 4000 mL/m^2 burned/day of fluids through evaporative losses.[112] Mechanisms of nonshivering heat production, and shivering remain intact in burn patients. However, Shivering increases metabolic requirements and is likely deleterious.

The induction of anesthesia results in relative ablation of thermoregulatory mechanisms and puts the patient at further risk for developing hypothermia. Patients under general anesthesia exhibit a markedly decreased threshold for responding to hypothermia (Figure 14.5). This is particularly important in burn patients given their high temperature set point and the deleterious effects of further stress responses and hypermetabolism in this patient population. Most anesthetics decrease nonbehavioral responses to hypothermia such as vasoconstriction, nonshivering thermogenesis, and shivering. Of course, behavioral responses are ablated during general anesthesia. Therefore, it is the responsibility of the intraoperative caregivers to monitor and maintain patient temperature.

Actions such as maintaining higher ambient air temperature, covering extremities and head, applying warm blankets, utiliz-

ing radiant heaters and forced air warming devices, warming fluids and blood, and warming gases are usually effective in maintaining core temperature if applied aggressively. Ideally, hypothermia should be corrected prior to transport to the operating room.[113] Hypothermia revealed in the preoperative evaluation may be due to inadequate resuscitation or metabolic instability. Either situation may predispose burn patients to intolerance of anesthetic drugs or the stress of surgery.

Pharmacological considerations

General considerations

Burn injury and its treatment result in physiological changes that may profoundly alter response to drugs. These changes alter both pharmacokinetic and pharmacodynamic determinants of drug response. Altered drug response in burned patients may require deviation from usual dosages to avoid toxicity or decreased efficacy.[114] The complex nature of the pathophysiological changes, interpatient variation in the nature and extent of burn injuries, as well as the dynamic nature of these changes during healing and recovery make it difficult to formulate precise dosage guidelines for burn patients. However, an understanding of the systemic response to large burn injuries can help predict when altered drug response can be expected and how to compensate.

The two distinct phases of cardiovascular response to thermal injury can affect pharmacokinetic parameters in different ways. During the acute or resuscitation phase the rapid loss of fluid from the vascular space due to edema formation results in decreased cardiac output and tissue perfusion. Volume resuscitation during this phase dilutes plasma proteins and expands the extracellular fluid space especially, but not exclusively, around the burn injury itself. Decreased renal and hepatic blood flow during the resuscitation phase reduces drug elimination by these organs. Also, decreased cardiac output will accelerate the rate of alveolar accumulation of inhalation agents, which may result in an exaggerated hypotensive response during induction of general anesthesia.

After approximately 48 hours, the hypermetabolic and hyperdynamic circulatory phase is established with increased cardiac output, oxygen consumption and core temperature. During this phase, increased blood flow to the kidneys and liver may increase clearance of some drugs to the point where increased doses are required.[115]

Many drugs are highly protein bound. Drug effects and elimination are often related to the unbound fraction of the drug which is available for receptor interaction, glomerular filtration, or enzymatic metabolism. The two major drug-binding proteins have disparate response to burn injury. Albumin binds mostly acidic and neutral drugs (diazepam or thiopental) and is decreased in burn patients. Basic drugs (pKa >8, propranolol, lidocaine, or imipramine) bind to α-acid glycoprotein (AAG). AAG is considered an acute phase protein and its concentration may double after burns. Since these drug-binding proteins respond in opposite ways to thermal injury it can be expected that changes in drug binding and function will depend on which of these proteins has the highest affinity for the drug in question. Martyn et al. observed decreased plasma albumin concentration and increased plasma AAG concentration in burn patients.[116] These observations were associated with an increased unbound fraction for diazepam (bound by albumin) and a decreased unbound fraction for imipramine (bound by AAG).

Volume of distribution (V_d) can be changed by alterations of either extracellular fluid volume or protein binding. Large changes in both of these variables occur with thermal injuries. Drugs with high protein binding and/or a V_d in the range of the extracellular fluid volume may be associated with clinically significant alterations of V_d in burned patients. V_d is the most important determinant of drug response following a rapid loading dose. However, adjustments in dose to compensate for altered V_d are indicated only when V_d for the drug is small (<30 1) because with larger V_d only a small fraction of the drug is present in the plasma.[114]

Clearance is the most important factor determining the maintenance dose of drugs and can influence the response to drugs given by infusion or repeated bolus during anesthesia. Drug clearance is influenced by four factors:

- metabolism;
- protein binding;
- renal excretion; and
- novel excretion pathways.

The characteristic hepatic extraction of a particular drug influences changes in its clearance that occur after thermal injury. Drugs vary greatly in their extraction by the liver. Hepatic clearance of drugs highly extracted by the liver depends primarily on hepatic blood flow and is insensitive to alterations in protein binding. Clearance of these drugs may increase during the hyperdynamic phase when hepatic blood flow is increased. In contrast, clearance of drugs that have a low hepatic extraction coefficient is not affected by changes in hepatic blood flow but is sensitive to alterations in plasma protein levels.[114] For these drugs it is the unbound fraction of the drug that is metabolized. As above, changes in unbound fraction depend on whether the drug is bound by albumin or AAG. Changes in protein levels produce clinically significant pharmacokinetic changes only for drugs that are highly bound (>80%).[117]

During resuscitation, renal blood flow may be reduced and renal excretion of drugs may be impaired. Later, during the hypermetabolic phase, renal blood flow is increased as a result of the elevated cardiac output. During this period excretion of certain drugs can be increased to the point that the dose may need to be increased. Loirat et al. reported increased glomerular filtration rates and reduced half-life of tobramycin in burn patients.[118] However, this was age-dependent and patients over 30 years of age did not have increased glomerular filtration or reduced half-life.

Burn patients may also experience altered drug clearance due to novel excretion pathways. Glew et al. found that 20% of a daily gentamicin dose was eliminated in the exudates lost to wound dressings.[119] In addition, rapid blood loss during surgery may speed elimination of drugs when blood loss and transfusion amount, essentially, to an exchange transfusion.

Hepatic clearance of drugs with low extraction coefficients is also sensitive to alterations of hepatic capacity (enzyme activity). There is evidence of impairment of hepatic enzyme activity in burn patients.[114] Phase I reactions (oxidation, reduction, or hydroxylation by the cytochrome P-450 system) are impaired in burn patients while Phase II reactions (conjuga-

tion) seem to be relatively preserved.[115] However, these generalizations do not always produce predictable alterations in pharmacokinetic parameters. For example, contradictory observations of morphine clearance in burn patients have been reported. Morphine metabolism is by glucuronidation. This is a Phase II reaction which is normally retained in thermally injured patients. Consequently, morphine clearance has been reported unchanged as predicted or decreased.[120,121] With so many variables involved, such as hepatic blood flow, V_d, plasma proteins, multiple drug exposure, and variation in burn injury, this inconsistency is not surprising. The key to effective drug therapy in burn patients is to monitor drug effects and carefully titrate the dose to the desired effect.

Muscle relaxants

In terms of anesthetic management, the most profound and clinically significant effect of burn injuries on drug response relates to muscle relaxants. Burn injuries of more than 25% total body surface area influence responses to both succinylcholine and the nondepolarizing muscle relaxants. In burned patients, sensitization to the muscle relaxant effects of succinylcholine can produce exaggerated hyperkalemic responses severe enough to induce cardiac arrest.[122–124] In contrast, burned patients are resistant to the effects of nondepolarizing muscle relaxants.[125–127] These changes are explained by up regulation of skeletal muscle acetylcholine receptors.[28–130]

Martyn and Richtsfeld[130] have recently reviewed the mechanisms of exaggerated hyperkalemic responses to succinylcholine. There are several disease states including burns, denervation, and immobilization that are associated with potentially lethal hyperkalemic responses to succinylcholine. The molecular mechanism appears to be both quantitative and qualitative changes in skeletal muscle postsynaptic nicotinic acetylcholine receptors. Animal and human studies consistently demonstrate an association of increased numbers of skeletal muscle acetylcholine receptors with resistance to nondepolarizing muscle relaxants and increased sensitivity to succinylcholine. In addition, the distribution of the new receptors is altered. Nicotinic receptors are normally restricted to the neuromuscular synaptic cleft but in these disease states new receptors are distributed across the surface of the skeletal muscle membrane. The new receptors are also a distinctly different isoform (α7AChR) that has been referred to as an immature, extrajunctional, or fetal receptor. The immature receptors are more easily depolarized by succinylcholine and their ion channel stays open longer. The immature receptors are also strongly and persistently depolarized by the metabolite of acetylcholine and succinylcholine, choline. It has been suggested that the hyperkalemic response to succinylcholine after burn or denervation injury results when potassium is released from receptor associated ion channels across the entire muscle cell membrane rather than just the junctional receptors. Depolarization persists because the channels stay open longer and the breakdown product of succinylcholine, choline, is also a strong agonist for the immature receptors.

Cardiac arrest in burned patients after succinylcholine administration was first reported in 1958.[122] It was not until 1967, however, that an exaggerated hyperkalemic effect was identified as the cause of this phenomenon.[123,124] Several clinical studies have documented exaggerated increases in potassium concentrations after succinylcholine administration in burned patients. However, considerable individual variability exists; only a few patients in these series developed dangerously high potassium levels. The size of the increase was greatest about 3–4 weeks after injury. The earliest exaggerated hyperkalemic response described occurred 9 days after injury and normal responses were observed in the remaining patients in this series for up to 14–20 days.[131] The shortest post burn interval associated with succinylcholine-induced cardiac arrest was 21 days.[132] Controversy surrounds recommendations regarding the safe use of succinylcholine after burn injury. Various authors recommend avoidance of succinylcholine at intervals ranging from 24 hours to 21 days after burn injury.[5,133] A series of letters to the editor of Anesthesiology from experts in this area illustrates the controversy surrounding this question.[134–136] It was pointed out by Martyn[136] that at the time when the mechanism of the cardiac arrest after succinylcholine was elucidated surgical treatment of burns was delayed for approximately 2 weeks until the eschar spontaneously separated. As a result there are few clinical data regarding potassium changes during this early period. On the basis of indirect evidence from experimental data, Martyn[136] recommended avoidance of succinylcholine starting 48 hours after injury. This seems rational and prudent. Brown and Bell[137] described super sensitivity of burned pediatric patients to the relaxant effect of succinylcholine. They observed more than 90% depression of muscle activity with 0.2 mg/kg succinylcholine without dangerous hyperkalemia. Despite these observations Brown and Bell state that it is generally advisable not to use succinylcholine in patients with large burns. The question remains: in the presence of life threatening laryngospasm in a burn patient, is it acceptable to give a small dose of succinylcholine (e.g. 0.1 mg/kg) and accept a theoretical risk of hyperkalemia to treat a real and immediate risk of asphyxia? There is not enough clinical evidence to answer this question conclusively and it remains a matter of clinical judgment.

When rapid sequence induction and quick onset of paralysis in burn patients is desired rocuronium is the drug of choice. A dose of 1.2 mg/kg of this drug provided good intubation conditions in 86 + 20 seconds in burned patients.[38] The problem with this choice is that muscle relaxation will persist for some time and precludes extubation after short cases and difficulty with intubation and ventilation may require emergent surgical airway access. A cyclodextrin (Org 25969) has recently been tested in man as a reversal agent with a novel mechanism of action for rocuronium.[138b] Org has been specifically designed to encapsulate rocuronium. This agent has been found to rapidly terminate neuromuscular blockade by rocuronium theoretically by sequestering it from nicotinic neuromuscular receptors. If this agent becomes approved for clinical use it may provide a way to rapidly reverse muscle relaxation with rocuronium and provide a more attractive choice for burn patients when rapid sequence induction is indicated.

Responses to nondepolarizing relaxants are also altered by burn injury. Three-to-five fold greater doses are required to achieve adequate relaxation.[125] Resistance is apparent by 7 days after injury and peaks by approximately 40 days. Sensitivity returns to normal after approximately 70 days. Two reports described slight but measurable resistance to nondepolarizing relaxants persisting for more than a year after

complete healing of the wounds. The mechanism of the altered response appears to involve pharmacodynamic rather than pharmacokinetic changes. Up regulated immature receptors are less sensitive to nondepolarizing relaxants. Burns greater than 25% total body surface area require higher total dose and greater plasma concentrations of nondepolarizing blockers to achieve a given level of twitch depression.[126]

Proliferation of acetylcholine receptors across the muscle membrane has been used to explain both resistance to nondepolarizing muscle relaxants and the exaggerated hyperkalemic response to succinylcholine.[30] The observation of resistance of a patient to metocurine for up to 463 days after burn has been used to suggest that hyperkalemic responses to succinylcholine also could persist for more than a year.[127] However, no pathologic hyperkalemic responses to succinylcholine in burned patients have been reported more than 66 days after burns.[133]

In contrast to other nondepolarizing neuromuscular blockers, mivacurium dosage requirements in pediatric patients appear to be unchanged by burn injury. The time to onset of drug action, degree of paralysis achieved by a specific dose, and rate of infusion required to maintain a given level of relaxation were all the same in burn patients as values reported for nonburned control patients.[134,135] Plasma cholinesterase activity is reduced in burn patients.[136] In a study by Martyn, the observation of an inverse relationship between plasma cholinesterase activity and recovery time from 25 to 75% twitch tension suggests that reduction of metabolic degradation of mivacurium may compensate for other factors that induce resistance to relaxants.[134,140] This observation suggests that mivacurium can be administered to burn patients in normal doses that would avoid cardiovascular perturbations associated with required larger doses of other relaxants in burn patients.

Anesthetic management

Airway management

If injuries do not preclude conventional airway management (i.e. mask fit, jaw lift, and mouth opening) standard induction and intubation procedures are appropriate. Hu et al. reported that gastric emptying was not delayed in patients with severe burns so that a rapid sequence induction is not necessary.[141] However, attention should be given to gastric residuals during enteric feeding. Development of sepsis can slow gastric emptying which can result in retained fluids in the stomach and risk of aspiration.

When burns include face and neck, swelling and distortion may make direct laryngoscopy difficult or impossible. In addition, loss of mandibular mobility may impair airway manipulation and make mask ventilation difficult. Fiberoptic intubation while maintaining spontaneous ventilation is a safe and reliable technique under these conditions. Fiberoptic intubation can be performed in awake adults but pediatric patients are unable to cooperate and must be sedated. Since most anesthetics cause collapse of pharyngeal tissues and airway obstruction they are unsuitable for fiberoptic intubation in patients whose airway would be difficult to manage with a mask.[142] Ketamine, however, is unique among anesthetic drugs because it maintains spontaneous ventilation and airway patency (Figure 14.6).[143,144]

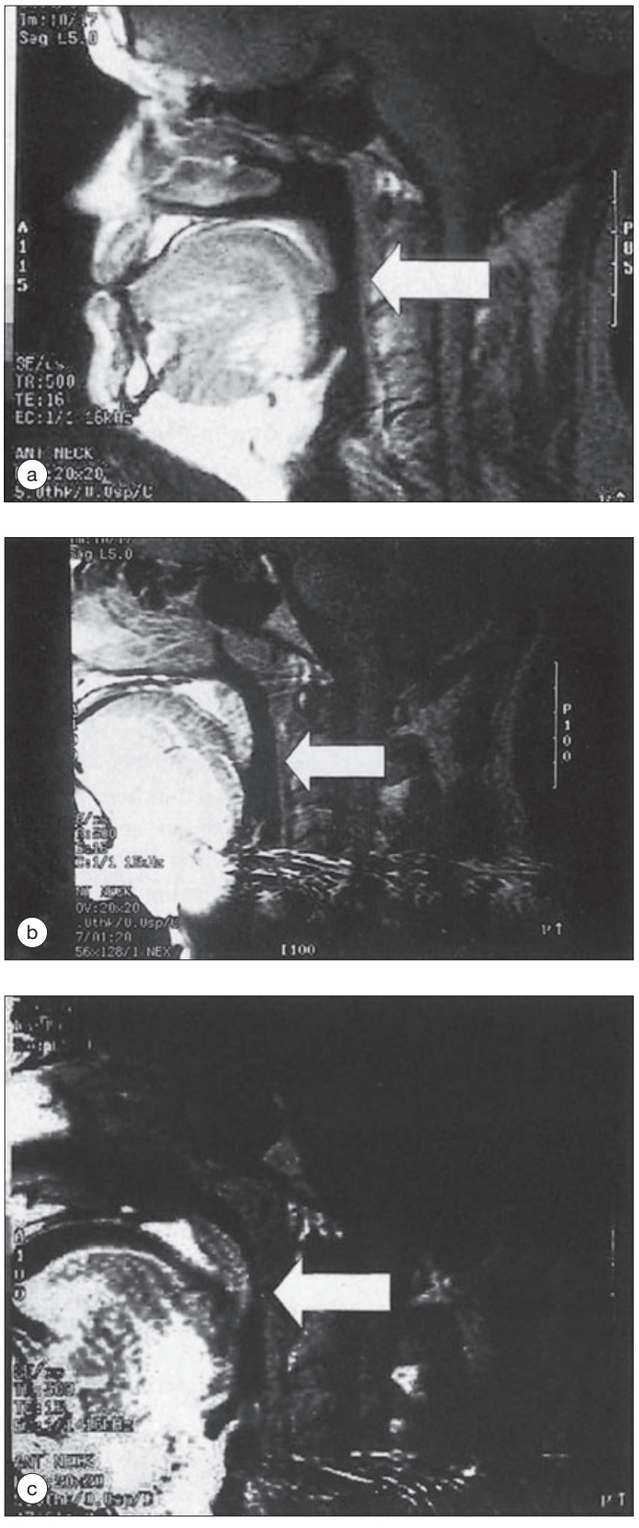


Fig. 14.6 Magnetic resonance images of a healthy volunteer during inspiration while conscious (a), or anesthetized with propofol (b) or ketamine (c). Anterior-posterior diameter of the pharynx at the level of the soft palate is marked by decreased during propofol anesthesia (b) but maintained during ketamine anesthesia (c).

Ketamine anesthesia has been found safe and effective for airway management in infants with difficult airways caused by congenital airway anomalies. Reports of successful nasotracheal intubation in infants with congenital airway malformations have been made both by manipulations guided by fiberoptic nasopharyngoscopy and the conventional technique of fiberoptic intubation with the endotracheal tube mounted on the fiberscope.[145,146] In the latter case an ultra-thin bronchoscope (2.7 mm) was required because a larger fiberscope would not fit through the appropriate-sized endotracheal tube. To facilitate intubation under ketamine anesthesia, topical anesthesia of the larynx with lidocaine prior to instrumentation of the larynx is advised. Since the ultra-thin bronchoscope lacks a working channel for administration of topical lidocaine, fiberoptic intubation with the 2.7 mm bronchoscope was preceded by nasopharyngoscopy with a 3.5 mm fiberscope for administration of topical lidocaine. At SBH Galveston we have also found this technique, utilizing two fiberscopes, effective in infants with burn injuries. Wrigley et al. evaluated the use of a 2.2 mm intubating fiberscope during halothane anesthesia in ASA 1 or 2 children aged 6 months to 7 years.[147] In this series of 40 patients a number of complications were experienced including laryngospasm and failure to achieve intubation with the fiberscope. This experience is in contrast to numerous reports of safe and effective airway management with ketamine.

Securing an endotracheal tube in a patient with facial burns presents a variety of problems and numerous techniques have been described.[148] Tape or ties crossing over burned areas will irritate the wound or dislodge grafts. A useful technique to avoid these problems involves the use of a nasal septal tie with one-eighth inch umbilical tape (Figure 14.7). The umbilical tape is placed around the nasal septum using 8 or 10 French red rubber catheters that are passed through each naris and retrieved from the pharynx by direct laryngoscopy and McGill forceps. A length of umbilical tape is tied to each of the catheters and when the catheters are pulled back through the nose, each end of the umbilical tape is pulled out its respective naris producing a loop around the nasal septum. Before securing with a knot, care should be taken to assure that the uvula is not captured in the loop. A knot in the nasal septal tie should be snug enough to prevent excessive movement of the endotracheal tube but loose enough to prevent ischemic necrosis of the underlying tissues.

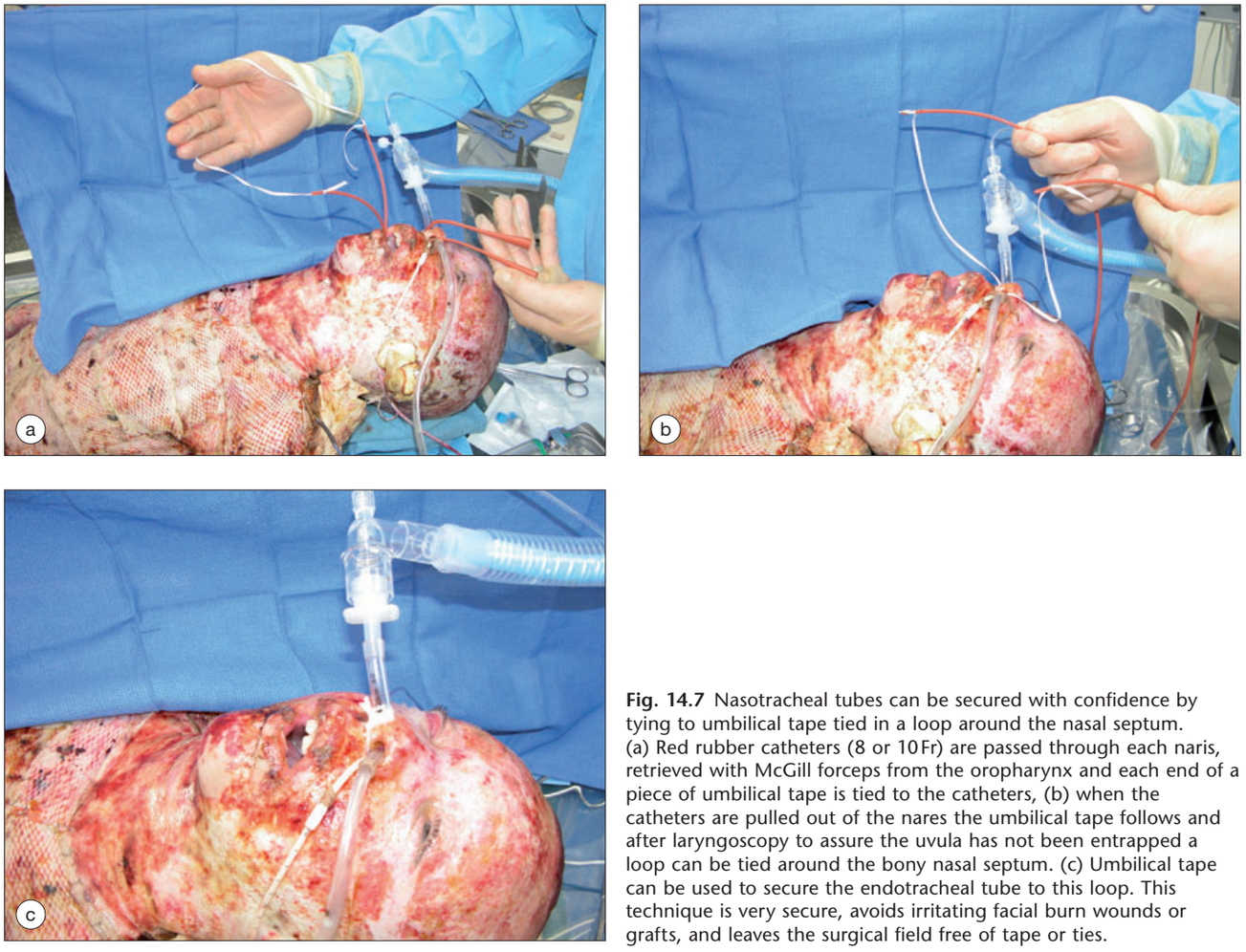


Fig. 14.7 Nasotracheal tubes can be secured with confidence by tying to umbilical tape tied in a loop around the nasal septum. (a) Red rubber catheters (8 or 10 Fr) are passed through each naris, retrieved with McGill forceps from the oropharynx and each end of a piece of umbilical tape is tied to the catheters, (b) when the catheters are pulled out of the nares the umbilical tape follows and after laryngoscopy to assure the uvula has not been entrapped a loop can be tied around the bony nasal septum. (c) Umbilical tape can be used to secure the endotracheal tube to this loop. This technique is very secure, avoids irritating facial burn wounds or grafts, and leaves the surgical field free of tape or ties.

Airway management using a laryngeal mask airway (LMA) has also been used successfully during burn surgery for children. McCall et al. reported their experience with 141 general anesthetics administered to 88 pediatric burn patients.[149] Nineteen (14.5%) of the procedures were complicated by respiratory events such as unseating, desaturation, and partial laryngospasm that required intervention. Two of these events required intraoperative intubation without sequelae, while all other events resolved with therapy. Interestingly, the presence of preoperative respiratory problems or face/neck burns did not predict intraoperative respiratory problems. These authors suggest that, in patients with upper airway mucosal injury, LMA airway management may help avoid further laryngeal injury that might occur with intubation of the trachea.

Hagberg et al. published a case report describing the successful use of an esophageal tracheal Combitube™ in a patient undergoing elective surgery for burn scars involving the mouth.[150] The patient had a Class IV oral airway by Samsoon and Young's modification of the Mallampati airway classification and limited mouth opening. A translaryngeal endotracheal tube was undesirable because tracheostomy had resulted in subglottic stenosis which could have been exacerbated by an endotracheal tube. After induction with fentanyl and propofol the Combitube™ was placed and the patient was relaxed with rocuronium and mechanically ventilated during the 60 minute procedure.

Monitors

As with any critically ill patient suffering from multiorgan system involvement, the choice of monitors in a burned patient will depend on the extent of the patient's injuries, physiological state, and planned surgery. In addition to the preoperative pathophysiology associated with thermal injuries, perioperative monitoring must be adequate to assess rapid changes in blood pressure and tissue perfusion associated with the massive blood loss that can accompany excision of burn wounds. The minimum standards of the American Society of Anesthesiologists require monitoring of circulation, ventilation, and oxygenation. Standard monitors include electrocardiography (EKG), measurement of systemic blood pressure, pulse oximetry, capnography, and inspired oxygen concentration. The ability to measure body temperature should be readily available and is highly recommended for the burn patient.

Standard EKG gel electrodes usually will not adhere to burn patients because the skin is injured or covered with antibiotic ointment. For acute burn surgery, surgical staples and alligator clips are useful. Respiratory rate can be quantitated using bioimpedance from the EKG signal or from the capnogram. Pulse oximetry in burn patients can be difficult when transmission pulse oximetry sites are either burned or within the operative field. Reflectance pulse oximetry has been suggested as an alternative in these circumstances.[151] However, an effective commercially available instrument has been slow in development.

If direct arterial pressure monitoring is not necessary, a blood pressure cuff can provide accurate measurements even if placed over bulky dressings applied to an extremity.[152] Systolic blood pressures obtained from the pressure at which the pulse oximetry signal returns during cuff deflation has also been found accurate.[153]

When blood loss is expected to be rapid and extensive, blood pressure may change more rapidly than the interval between cycles of noninvasive blood pressure measurement. In this case an arterial catheter can provide direct and continuous measurement of blood pressure. This monitor can provide much more information regarding the patient's circulatory status than just systolic and diastolic blood pressure. The arterial pressure wave form is influenced by preload, contractility, and vascular tone. Perioperative variation in the rate of rise of arterial pressure, the area under the pressure wave, position of the dicrotic notch, and beat to beat alterations in systolic pressure related to respiration all reflect clinically significant hemodynamic changes.[154] With experience, trends in these variables can help guide volume and vasoactive therapy. Display of the beat to beat arterial pressure allows measurement of systolic pressure variation (SPV). SPV is the difference between maximum and minimum systolic blood pressure during a single cycle of positive pressure mechanical ventilation. Several studies have correlated SPV with cardiac output response to volume infusion. Tavernier et al. reported that in septic patients on mechanical ventilation, SPV is a better predictor of left ventricular ejection volume response to volume loading than either pulmonary artery occlusion pressure or echocardiographic measurement of left ventricular end diastolic area.[155] Measurements are not as simple as merely 'eyeballing' the blood pressure trace because several variables influence SPV, including arrhythmias, tidal volume, and mechanical versus spontaneous ventilation. SPV provides a dynamic assessment of the interaction of preload and cardiac output.[156]

Arterial blood sampling for blood gas analysis also provides valuable information regarding pulmonary function and acid-base balance. Inadequate tissue perfusion may manifest as metabolic acidosis despite apparently adequate arterial and central venous blood pressures.

In patients with large burns a central venous catheter serves several functions. Central venous pressure can be useful for titrating blood and fluid administration. Blood samples from a central vein are not truly mixed venous but trends in central venous oxygen tension can help identify inadequate tissue perfusion. A central venous catheter sutured into place also provides very secure intravenous access and is an ideal route for administration of vasoactive infusions. A pulmonary artery catheter is usually not required for burn surgery. In some cases, however, the ability to more closely monitor ventricular function and oxygen supply/demand relationships may be helpful as when large doses of inotropes or high PEEP is required. As described above, a newer transpulmonary thermodilution catheter system is also capable of estimating thoracic and end diastolic cardiac blood volumes. These measures of preload have been reported to correlate better than filling pressures (central venous pressure or pulmonary artery occlusion pressure) with changes in cardiac index or oxygen delivery with fluid volume administration.

Urine output is the most useful perioperative monitor of renal function. Urine output of 0.5–1.0 mL/kg/h is often recommended as an end point for fluid management in acute burn patients. Adequate urine output is one measure of both renal and global perfusion. When intraoperative transfusion is planned, examination of the urine may be the only reliable

indicator of a transfusion reaction since signs and symptoms other than hematuria are masked by general anesthesia or hemodynamic changes associated with burn surgery. Myoglobinuria may also occur after burn injury and in this case a Foley catheter is necessary to monitor response to therapy. Diuretic therapy for myoglobinuria or any other indication will negate the usefulness of urine output as an index of perfusion.

Vascular access

Securing adequate vascular access in the acutely burned patient is one of the more technically challenging procedures facing the anesthesia care team. In the pediatric age group the task can be even more difficult. Skin sites for insertion of vascular access catheters may be involved in the burn, and regional anatomy is often distorted by burn, edema, or scarring. Early in the course of an acute burn, shock leads to vasoconstriction, making cannulation of peripheral vessels nearly impossible. Later, once the patient has had several operative procedures, scarring in the area of access sites makes their placement difficult as well. Since burn patients undergo multiple debridement procedures it is necessary to attain vascular access many times in each patient. The need for frequent catheter changes between procedures to minimize catheter-related sepsis compounds the problem. The anesthesia care team is frequently involved in the maintenance of adequate vascular access during the period of acute care and therefore must be facile in their placement. When a large portion of the surface area is burned, it becomes necessary to insert catheters through burned skin. Sutures are typically necessary to secure these catheters. If the burn is deep, it may have to be debrided prior to line placement so that the catheter can be sutured to viable tissue.

For the operative excision of a large burn wound, an arterial catheter allows continuous blood pressure monitoring in the face of sudden and sometimes massive blood loss as well as during the titration of vasoactive drugs. It also allows easy access to blood samples for arterial blood gases, chemistries and serial hematocrit determinations. For pediatric patients with large burns, arterial monitoring is essential. Achieving arterial access is often complicated by overlying burn, skin graft, or scarring. In the latter case palpation of pulses can be difficult and the use of a Doppler probe is often very helpful.

The radial artery is the most frequently used site for monitoring non burned patients, with large numbers of patients cannulated without complications.[157] There is a relatively high rate of arterial occlusion: 8% with 20-gauge catheters and 34% with 18-gauge, but almost all completely recanalize.[158] Clearly, however, the catheter must be removed if distal hand or digit ischemia develops. In patients with severe hypotension the radial artery is not always easy to cannulate and blood pressure readings from the vessel can be inaccurate. Additionally, it is often difficult to maintain a radial arterial catheter in burn patients for more than 48 hours, particularly in pediatric patients, and, unfortunately, the hands and forearms are typically involved in a large burn wound.

Accessing the femoral artery is easier in most patients, particularly those in low perfusion states because it is a larger and more central vessel.[159,160] The groin is often spared from injury, even in a large burn, and placement of a catheter in the femoral artery is not affected greatly by the presence of edema.[161] The duration of patency is longer than that of a radial artery catheter, and the incidence of infection in a femoral artery catheter is similar to that of any other location, about 1%.[159] The risk of mechanical complications is smaller than that of more peripheral arteries because the arterial/catheter diameter ratio is larger. Still some recommend avoiding the femoral site unless no other site is available since loss of limb, or limb length discrepancy in children, is a devastating, if rare, complication.[162]

Other sites for arterial access include the dorsalis pedis, posterior tibial, and temporal arteries, none used with great frequency, and all distal enough to give inaccurate blood pressure readings, particularly in hypotensive patients. Use of the axillary artery has the disadvantages of a relatively higher rate of infection and difficulty in maintaining correct arm positioning for proper catheter function.[163]

The incidence of complications from arterial catheters has been cited as anywhere from 0.4 to 11%, with the higher rate seen most often in pediatric patients, particularly those under 1 year of age.[164–166] Early complications include bleeding, which is usually easily controlled, and hematoma formation, which is more common if the artery is transfixed during cannulation and is avoided by an adequate period of pressure applied to the site if bleeding occurs. Damping of the arterial waveform or clotting of the catheter is more common with small catheters or small arteries; this can be lessened somewhat by continuous heparin flushing systems.[167]

The incidence of catheter-related infections with arterial catheters is generally low, quoted at anywhere from 0.4 to 2.5% until 4 days duration. The incidence of infection gradually increases to 10% by 7 days, but stays constant thereafter. This relatively low rate of infection in comparison to central venous catheters confirms the clinical impression that catheter-related infections are less commonly seen in the high-flow arterial system.[162,168]

Vascular insufficiency of the distal extremity occurs in 3–4% of patients in whom arterial catheters are placed.[163] Fortunately, most cases of ischemia resulting from vascular obstruction are evident immediately and resolve when the catheter is removed. The risk of ischemia can be minimized by selecting the smallest possible catheter that will give an accurate arterial waveform.[161] There is a marked increase in the incidence of arterial vasospasm when over 50% of the vessel lumen is occluded by the catheter.[169] This is certainly more of a problem in pediatric patients than adults. Predisposing factors to ischemia from arterial obstruction include hypotension, the use of vasoconstrictors, prolonged catheterization, age under 5 years, and insertion by cutdown.[170] Indeed, most reports of chronic sequelae have come in patients less than 1 year of age who were hypotensive at the time of catheter insertion. Other less commonly reported complications from arterial catheters include cutaneous damage, pseudoaneurysm formation, and septic arthritis of the hip.[171–173]

Central venous catheters are very useful for large volume resuscitation in patients with burns over 30% or more of their TBSA. As with arterial catheters, burn wound, edema, and scarring all hamper the placement of central venous catheters. Normal anatomic landmarks can be totally obliterated. The problem is compounded by the need for long-term access in

patients with large burns who are also at high risk for central venous catheter infections and so will require frequent line changes. Ultrasound guidance has been used successfully to guide correct placement of appropriate-size catheters into central veins but is less helpful for the subclavian approach and extensive scarring from burn wounds can degrade the ultrasound image.

Catheters placed in the subclavian vein have a lower risk of infection than those placed in the internal jugular or femoral vein, but carry a higher risk of mechanical complications during their placement.[174] The internal jugular vein is typically more difficult to access in burn patients with facial and neck burns or edema and is associated with a higher infection risk. Additionally it is a difficult position in terms of patient comfort, particularly for pediatric patients. The femoral vein is a large central vein that is usually easy to cannulate. It has several advantages including no risk of pneumothorax, easier control of bleeding, less anatomic distortion due to edema, and the inguinal region is often spared even in a large burn. The risk of catheter-related infection is higher in the femoral vein than at other vascular access sites in some studies, and the risk of venous thrombosis is also quoted by some authors as being greater.[175–177]

Early complications with the placement of venous catheters include trauma, hematoma, bleeding, air embolus, pleural effusion, pneumothorax, or pericardial tamponade. Delayed complications include infection and thrombosis, which have been studied by many authors with often conflicting results. In one trial, 45 patients were randomized to either an upper extremity catheter group in which catheters were placed in the internal jugular or subclavian vein, or to a lower extremity catheter group in which catheters were placed in the femoral vein. No patients in the upper extremity group developed thrombosis, while six patients (25%) in the lower extremity group developed deep vein thrombosis. Additionally, another seven patients (29%) in the lower extremity group had nondiagnostic ultrasound findings.[177] In another trial involving pediatric patients, mechanical complications occurred in 9.5% of femoral venous catheters but only 1.8% of nonfemoral catheters.[178] A third study involved 162 femoral venous catheters and 233 nonfemoral venous catheters; mechanical complications were equal in the two groups, 2.5% versus 2.1%. However, three of four patients who developed thrombosis were in the femoral group, as was the one patient who developed an embolus.[176] Conversely, 1449 femoral venous catheters were maintained in 313 burn patients with no pulmonary emboli. These catheters were changed every 3 days and the authors maintain that the femoral site can successfully be used as part of a site rotation for central venous access in burn patients.[179] Another 224 pediatric burn patients with femoral venous catheters had only a 3.5% incidence of mechanical complications including only one thrombus.[180] Finally, there has been a 20–46% incidence of femoral venous thrombosis found at autopsy in patients with femoral venous catheters left in place for a week or longer. A 67% incidence of thrombotic complications has been reported with internal jugular catheters and 61% with umbilical venous catheters when studied at autopsy.[181] It would seem safe to say that the femoral vein can be used for catheterization for short intervals with frequent line changes and diligent monitoring for thrombotic complications.[182]

When looking at the incidence of catheter-related infection from central venous catheters in burn patients, the answer is even less clear. There is an inherent difficulty when talking about the incidence of catheter-related infection in burn patients for several reasons. First, the patients with central venous catheters are the sickest patients. Secondly, the burn wound is a constant source of infection and pneumonia, and urinary tract infections are also fairly common in critically ill burn patients; in many patients catheter-related infection is a diagnosis of exclusion but burn patients always have at least one other obvious source of infection. Finally, since most catheter-related infections develop when bacteria migrate down the catheter tract from the skin, there is a higher risk of catheter infection when the insertion site is through or very near a burn wound.[183,184] To further cloud the picture, differing definitions of catheter-related infection make comparing different studies of the problem more difficult. Catheter-related infection in burn patients has been reported to have an incidence as low as 2.5% and as high as 22.4%.[183] One large study of 1183 burn patients and 1346 central venous catheters showed that the incidence of catheter-related infection was 19.5% with a mortality of 14.1%. These authors cite catheter-related infection as the second most common cause of sepsis in the burn patient after the burn wound.[185]

Many older studies recommend frequent catheter changes to decrease the incidence of infection, but several studies show no increase in infection out to as many as 7–10 days. Three large randomized trials demonstrated no difference in the incidence of catheter-related infections among groups who had lines placed at a new site every 7 days and groups who had their lines changed over a guidewire every 7 days.[175,186,187] The incidence of mechanical complications is clearly lower with guidewire exchange rather than changing to a new site. Several other trials have also indicated no advantage to routine changing of catheters before 7–10 days.[180,188,189] There are conflicting data in relation to incidence of infection and the site of the central venous catheter, although almost all studies agree that the incidence of infection is lowest if the subclavian approach is used.[175,178,189,190] Also, all studies that compared single lumen and multilumen catheters found a lower rate of infection with single lumen catheters.[174,189,190] Those that compared percutaneous catheter placement with placement via cutdown technique found a higher incidence of infection with cutdowns.[189–191]

Advances in vascular catheters that incorporate an antibiotic have improved the efficacy of these devices in reducing the incidence of catheter related bloodstream infections. A recent prospective, randomized trial examined the efficacy of two types of central venous catheters that incorporate antibiotics: one catheter releases silver ions continuously and the other is impregnated with two antibiotics with different mechanisms of action, rifampicin and minocycline. Both catheters were associated with low rates of catheter related blood stream infections.[192] Improvements in this technology would provide two significant clinical advantages. Reduced colonization of central venous catheters will reduce blood born infections and reduced need for changes in vascular access sites for infection control will reduce the incidence of mechanical complications of catheter insertion.

Additional measures recognized by the CDC for reducing catheter related blood stream infections include maximum

sterile barrier technique (cap, mask, sterile gown, sterile gloves, and large sterile drape with a small opening).[193] A meta-analysis concluded that chlorhexidine gluconate is superior to providone-iodine for insertion-site disinfection.[194]

The operative debridement of a large burn wound is accompanied by rapid and sometimes considerable blood loss. Critical hypoperfusion of vital organs begins to occur when 20–30% of the blood volume is lost.[195] Irreversible shock and cellular damage can begin to occur within minutes depending on the continuing rate of loss. The achievement of a very rapid fluid infusion rate is critical in the resuscitation of the patient undergoing operative excision of the burn wound. Clearly, adequate venous access to achieve rapid infusion rates is imperative.

The laminar nonpulsatile flow of fluid through a tube was described by Poiseuille and is expressed by the formula:

$$Q = ?P?r^4/8?L$$

where Q is flow, ΔP is the pressure differential in the tube, r is the radius of the tube, ? is viscosity of the fluid, and L is the length of the tube. From this formula, several relationships are established (Table 14.7). Flow through a tube can be increased by high pressure gradients, tubes of large diameter and short length, and the use of low-viscosity fluids. The most significant variable is the radius of the tube where changes result in exponential changes in flow: doubling the diameter of the tube increases flow 16 times. There have been a number of studies comparing flow rates of various catheters under different conditions. It is difficult to compare these studies directly since methods are not standardized. However, it is possible to gain from them valuable insight about the factors affecting flow. Large diameter, short catheters maximize flow, as does a central venous location: flow is 20–40% less in a peripheral vein than in a central vein for the equivalent diameter and length catheter. Peripheral veins add resistance to flow before fluid is delivered to the central compartment.[196] Flow rates, however, are equal in hypovolemia and normovolemia for the same catheter size and length.

The high viscosity of blood diminishes flow rates considerably. Diluting one unit of packed red blood cells with 250 mL of normal saline can increase the flow of the blood by tenfold.[197] The application of a 300 mmHg pressure device to the blood unit can increase the flow rate another seven times. The diameter and length of the intravenous tubing system delivering fluid from the bag to the patient has profound effects on the rate of fluid delivery. Large-bore trauma tubing with an internal diameter of 5.0 mm allows fluid to flow three times as fast as standard blood infusion set tubing with an internal diameter of 4.4 mm, which is twice as fast as standard intravenous tubing with an internal diameter of 3.2 mm. The largebore trauma tubing allows fluid flow rates of 1200–1400 mL/min.[198] Also, infusing blood or fluid through a 'piggyback' system into another access line can decrease flow by up to 90%

Several large studies have shown introducer catheters to be superior to all other devices for the rapid infusion of blood and intravenous (IV) fluid (Tables 14.8 and 14.9). These catheters are typically of large diameter, with thin walls and no tapering so that for any given catheter size the inner diameter is largest.[195,199,200] This finding holds especially true for pediatric patients where vessel size is limited. The flow rate of a 4-French introducer catheter is greater than a 16-gauge IV catheter. However, the 4-French introducer, placed by the Seldinger technique, requires only a 21-gauge needle to be inserted into the vein for its placement.

TABLE 14.8 INTRODUCER CATHETER SIZES AND FLOW RATES (FLOW RATES FOR NORMAL SALINE UNDER GRAVITY)

Catheter size	Patient size	Flow rate
4 French	5–10 kg	285 mL/min
5 French	10–15 kg	380 mL/min
6 French	15–20 kg	480 mL/min
7 French	>20 kg	585 mL/min
8.5 French	>40 kg	805 mL/min

TABLE 14.9 INTRAVENOUS CATHETER SIZES AND FLOW RATES (FLOW RATES FOR NORMAL SALINE UNDER GRAVITY)

Intravenous catheter	Flow rate
24 gauge	14 mL/min
22 gauge	24 mL/min
20 gauge	38 mL/min
18 gauge	55 mL/min
16 gauge	75 mL/min
14 gauge	93 mL/min

When planning vascular access for perioperative anesthetic management it is important to be aware of and take into account the patient's hospital course. Choice of access site should avoid vessels previously involved in complications such as thrombosis or vascular injury. Note must be taken of when existing catheters were placed and what the local convention is with regard to timing of regular changes of access sites for infection control. The patient's hospital course must also be considered when choosing a catheter. Although introducers offer the greatest flow and may provide the anesthesiologist a sense of assurance, the patient may require continuous vascular access for months of hospitalization and may return for surgery weekly. Large vascular introducers placed weekly will not be tolerated without complications that may result in morbidity and will limit access sites for future surgery. The catheter should be large enough to transfuse appropriately for the case but catheters much larger will increase risk without benefit.

Patient transport

The safe transport of a critically ill burn patient to and from the operating room can be a formidable task. A methodical approach will help to insure patient safety and the seamless maintenance of respiratory, hemodynamic, and general support. Hemodynamic status should be optimized prior to patient transport; pharmacological support may be required. The American Society of Anesthesiologists standards mandate evaluation, treatment, monitoring and equipment appropriate to the patient's medical condition for any transport. Depending on the patient's condition, simple observation may be

appropriate. Patients requiring supplemental oxygen should be monitored by pulse oximetry. Hemodynamic monitoring is guided by the patient's hemodynamic status. Sufficient battery power must be available for uninterrupted monitor and infusion pump function during transport.

Airway supplies should be readily available including a full oxygen cylinder, a self-inflating Ambu bag with mask, and intubation equipment. The patient's airway and ventilation as well as overall condition must be continually observed by the anesthesia care team. Drugs for resuscitation should accompany the patient on any transport. As discussed below, hypothermia is poorly tolerated by patients with an acute burn injury. It is imperative that patients be kept warm during transport in order to avoid increasing oxygen consumption and taxing limited metabolic reserve.

Selection of anesthetic agents

Many anesthetic agents have been used effectively for the induction and maintenance of anesthesia in burn patients. Intravenous agents (Table 14.10) can be used for both induction and maintenance and the specific agent used will depend primarily on the patient's hemodynamic and pulmonary status as well as the potential difficulty in securing the patient's airway. Ketamine has many advantages for use in the burn patient for induction and maintenance of anesthesia. As an induction agent, ketamine can be administered at a dose of 0.5–2.0 mg/kg. Except in patients that are catecholamine-depleted, ketamine generally preserves hemodynamic stability (Figure 14.8). In addition, ketamine preserves hypoxic and hypercapnic ventilatory responses and reduces airway resistance.[201] Compared to other IV anesthetics, airway reflexes remain more intact after ketamine administration. However, some risk of aspiration remains. Patients who do not require ventilatory support can be allowed to breathe spontaneously, which provides an additional margin of safety should inadvertent extubation occur. In fact, some clinicians have reported the use of ketamine anesthesia without instrumentation of the airway.[202,203] Patients were allowed to breath spontaneously and the airway complication rate was comparable to that of intubated patients. The use of intramuscular ketamine can be beneficial in securing the airway in pediatric burn patients or uncooperative adults who do not have vascular access. Because ketamine preserves spontaneous ventilation and induces dissociative anesthesia, it provides good conditions for securing the airway by fiberoptic bronchoscopy. Addition of other anesthetic agents, particularly potent volatile agents or opioids, should be avoided until the airway is secured because these anesthetics depress respiratory drive and relax pharyngeal muscles thus increasing the risk of apnea, upper airway obstruction, or laryngospasm. Ketamine can also be utilized, either alone or in combination with other anesthetics, for maintenance of anesthesia either by infusion or intermittent bolus. Ketamine has potent analgesic properties and is used extensively in the operating room as well as for painful dressing changes and patient manipulations. A drying agent such as glycopyrrolate (2–5 g/kg) is commonly given in combination with ketamine to reduce ketamine-induced secretions. In addition, benzodiazepines are often recommended in older children and adults to reduce the incidence of dysphoria sometimes associated with ketamine administration. Induction agents such as thiopental or propofol are more commonly used in patients returning for reconstructive procedures rather than in the acute phase of injury but are also sometimes chosen in patients with small burns and no evidence of airway or facial involvement when direct laryngoscopy is planned.

TABLE 14.10 DOSAGE GUIDELINES FOR THE MOST COMMONLY USED INTRAVENOUS ANESTHETIC INFUSIONS

	Infusion rate		
Anesthetic	**Loading dose (mg/kg)**	**Maintenance of anesthesia* (mg/min)**	**Sedation (mg/min)**
Thiopental	2.0–4.0	10–20	1.0–5.0
Methohexital	1.5–3.0	5.0–8.0	0.5–2.5
Midazolam†	0.2–0.4	0.1–1.0	0.035–0.7
Etomidate	0.2–0.4	1.0–2.0	0.5–1.0
Propofol	1.5–2.0	4.0–12.0	2.0–5.0
Ketamine‡	0.5–1.0	0.7–5.4	1.0–2.0

*Adjuvant to other agents (i.e. nitrous oxide, opioids).
†Infusion rate for midazolam is highly variable. Values in the table represent more commonly used doses.
‡Ketamine is contraindicated in head-injured patients. Its inclusion in this table pertains to use in other injuries.
From Nolan JP. Intravenous agents. In: Grande CM, et al., eds. Textbook of trauma anesthesia and critical care. St Louis: Mosby Year Book; 1993.

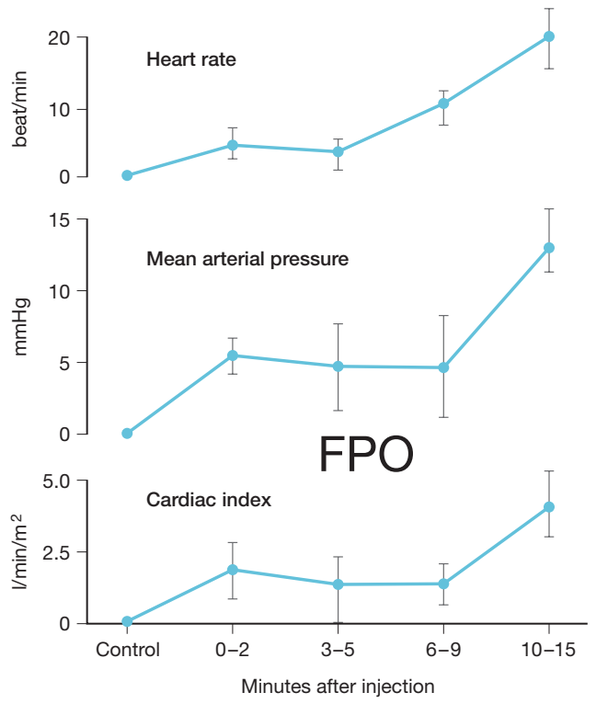


Fig. 14.8 Heart rate, mean arterial pressure and cardiac index changes during a 15 minute period of ketamine administration to critically ill patients. (From: Nolan JP. Intravenous agents. In Grande CM, et al., eds. Textbook of trauma anesthesia and critical care. St. Louis: Mosby Yearbook; 1993.)

Volatile anesthetics may be used for both induction and maintenance of anesthesia in burn patients. In pediatric patients, mask induction with either halothane or sevoflurane is commonly used if the patient does not have injuries that may make airway manipulation difficult. In the acute setting, an anesthetic technique involving nasotracheal intubation after mask induction with halothane, nitrous oxide, and oxygen has been described.[204] The proponents particularly emphasize avoiding the potential problems associated with the ketamine-based technique. However, volatile agents produce dose-dependent cardiac depression and vasodilation (Table 14.11). In addition, hypoxic ventilatory drive is ablated by volatile anesthetics at low concentrations and a dose-dependent depression of hypercapnic drive also occurs. However, as maintenance agents volatile anesthetics have predictable wash-in and wash-out kinetics (Figure 14.9) and provide a useful adjunct to other agents when titrated to hemodynamic and ventilatory parameters. Of the volatile agents, nitrous oxide has the least impact on cardiovascular and respiratory function and can serve as a useful component of a balanced anesthetic if the patient's oxygen requirements permit (Table 14.11).

Opioids are important agents for providing analgesia for burn patients throughout the acute phase of injury and for providing postoperative analgesia in patients undergoing reconstructive procedures. The spectrum of opioids currently available provides a wide range of potencies, durations of action, and effects on the cardiopulmonary system (Table 14.12). Burn patients experience intense pain even in the absence of movement or procedures, and opioids are the mainstay for providing analgesia in the acute phase of burn management. However, acute burn patients usually become tolerant to opioids because they receive continuous and prolonged administration of these drugs. Therefore, opioids should be titrated to effect in the acute burn patient. Most opioids have little effect on cardiovascular function but they are potent respiratory depressants. Therefore, the ventilatory status of patients receiving opioids, particularly those with challenging airways, should be monitored closely.

Regional anesthesia can be used effectively in patients with small burns or those having reconstructive procedures. In pediatric or adult patients having procedures confined to the lower extremities, lumbar epidural or caudal anesthesia can provide a useful adjunct for control of postoperative pain. In cooperative adult patients with injuries confined to lower extremities, epidural or intrathecal anesthesia may be used if no contraindications exist. For upper extremity procedures,

TABLE 14.11 CARDIOVASCULAR EFFECTS OF INHALATION AGENTS

Effect	Halothane	Enflurane	Isoflurane	Sevoflurane	Nitrous oxide
Contractibility	↓↓	↓↓	↓	↓	±
Cardiac output	↓↓	↓↓	±	±	±
Systemic vascular resistance	±	↓	↓↓	↓↓	±
Mean arterial pressure	↓↓	↓↓	↓↓	↓↓	±
Heart rate	↓	±	↑↑	↑↑	±
Sensitization to catecholamines	↑↑↑	±	±	±	±
Baroreceptor reflexes	↓↓↓	↓↓↓	↓	↓	±

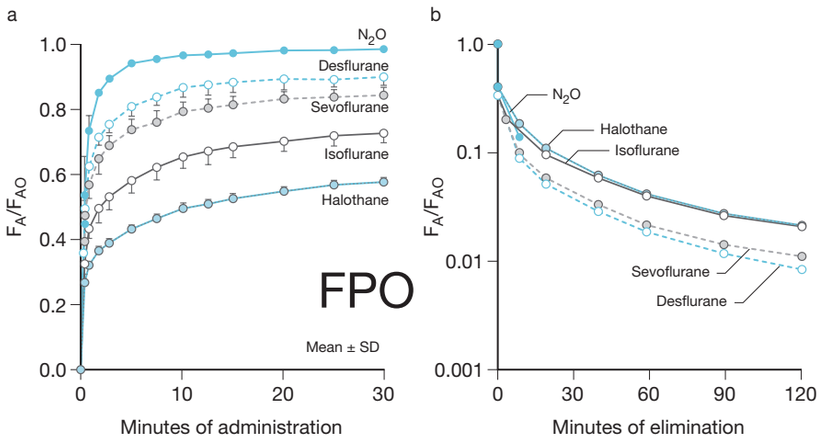


Fig. 14.9 (a) Washin curves of a variety of inhalation anesthetics. (b) Washout curve for volatile anesthetics. (From: Yasuda N, et al. Comparison of kinetics of sevoflurane and isoflurane in humans. Anesth Analg 1991; 72:316–324.)

TABLE 14.12 CLINICALLY RELEVANT CHARACTERISTICS OF THE FIVE MOST COMMONLY USED OPIOIDS

	Morphine	Meperidine	Fentanyl	Sufentanil	Alfentanil
Relative potency	1.0	0.1	100–200	700–1200	30–60
LD_{50} in dogs (mg/kg)	200	700	10	4.0	59.5–87.5
Analgesic dose	70–210 g/kg	0.7–2.1 mg/kg	1.0–2.0 g/kg	0.25 g/kg	4.8 g/kg
Anesthetic dose*	0.5–3.0 mg/kg	3.0–10 mg/kg	50–100 g/kg	5.12 g/kg	100–300 g/kg loading dose +25.50 g/kg/h
MIC_{50}			15 ng/mL		270–400
MIC_{90}			25 ng/mL		
MIC_{95}			30 ng/mL		
Cardiovascular stability	±	−−	++++	++++	+++
Histamine release	++	+++	–	–	–
Respiratory depression	++	++	+++	+++	+++
Elimination half-life (h)	3.0	2.5	3.5	2.5	1.5

LD_{50} the dose that is lethal in 50% of subjects; $MIC_{50,90,95}$ minimum intra-arterial concentration that prevents response to sternotomy incision in 50%, 90%, and 95% of patients; –, no; +, yes.
*Doses used for cardiac surgery. Smaller doses combined with other drugs are sufficient for most trauma patients.
From Capan LM, et al. Principles of anesthesia for major trauma victim. In: Capan LM, et al., eds. Trauma Anesthesia ••.

brachial plexus block may be considered as the primary anesthetic or as an adjunct for postoperative pain control.

Scalp donor sites are particularly painful. Sensory nerves to the scalp are superficial and easily blocked with injections of local anesthetic and this technique has been used for awake craniotomy.[205] Scalp blocks have been used with success at our institution for donor sites in acute patients (unpublished observation) and for scalp procedures in reconstructive patients.[206]

Fluid management

Fluid management and blood transfusion for burn wound excision can be quite challenging. Fluid administration should be guided not only by intraoperative events but previous hospital course and ICU treatment goals. If early excision is performed during the first 24 hours perioperative fluid management may involve the acute resuscitation and fluid needs will exceed replacement of shed blood. Even after this period insensible fluid requirements are increased by large open surfaces from excised wounds, hypermetabolic state and hyperthermia. However, early in the patients' hospital course patients are edematous from the large amounts of crystalloid solutions administered during resuscitation. At this time additional crystalloid administered during the perioperative period may be poorly tolerated and may result in complications of compartment syndrome in extremities or the abdomen. After the initial period of resuscitation ICU therapy may include vigorous attempts to reduce edema including the use of diuretics. If the ICU staff have been administering diuretics to the patients all week in order to reduce interstitial edema it is not helpful when the patient receives several liters of fluid in the operating room. Perioperative fluid management must also take into account hypotonic clysis fluids that the surgeons may inject to facilitate donor skin harvest with the dermatome. In small children the volume of this fluid can be in excess of 50 mL/kg. State of hydration and electrolyte balance must be monitored carefully in order to maintain proper fluid balance.

Replacement of surgical blood loss during burn wound excision and grafting can be just as challenging. Unlike most general surgical procedures, during burn surgery it is impossible to accurately estimate the amount of shed blood. Shed blood is not collected in suction canisters where it can be measured. During burn surgery shed blood is concealed beneath the patient, in drapes, in sponges, or may be washed down a drain on the operating table. As discussed above regarding the initial resuscitation, there is no one physiological end point to titrate volume replacement. Arterial pressure may be maintained by vasoconstriction despite significant hypovolemia, central venous pressure is not a reliable index of preload, changes in urine output and hematocrit lag behind rapid reductions in blood volume, and metabolic acidosis may indicate deficient perfusion but does not identify the specific problem. All of these variables are useful, however, when evaluated together. Although, systolic blood pressure may be within the normal range, alterations in the arterial wave form and changes with the respiratory cycle may indicate hypovolemia. Even though central venous pressure correlates poorly with hemodynamic function, this variable is useful in determining if volume administration will be tolerated by the patient. If perfusion appears inadequate and central venous pressure is low or normal it is safe to give volume. If central venous pressure is elevated, volume administration may cause pulmonary edema.

The concept of transfusion trigger with regard to burn care is discussed below. It must be remembered, however, that during rapid blood loss the hematocrit may change much

slower than the blood loss and often blood must be administered before the hematocrit falls below a specific trigger.

Blood transfusion

The need for blood transfusion is usually not a major concern during the immediate resuscitation phase in acutely burned patients unless other coexisting trauma exists. Nevertheless, a fall in plasma hemoglobin concentration can occur during the acute resuscitative phase due to hemodilution and blood loss from escharotomies and other invasive procedures.[207] However, major blood loss is common when patients are taken to the operating room for excision and grafting of burn wounds. Desai and colleagues reported that the amount of blood loss during burn wound excision is determined by the age of the burn, the body surface area involved and whether infection is present (see Table 14.4).[10] In general, more blood loss was observed as the time from initial injury increased and if wounds were infected. Transfusion requirements ranging from 0.45 to 1.25 mL of packed red blood cells (PRBCs) per cm^2 burn area were reported. In another study, Criswell and Gamelli[2] reported an average transfusion rate of 0.89 mL PRBC/cm^2 burn area in a cohort of adult burn patients. A study by O'Mara and colleagues showed an average transfusion rate of 0.65 mL PRBC/cm^2 in a heterogeneous group of burn patients.[208]

Controversy exists regarding transfusion triggers and targets. Some authors advocate allowing hematocrit to drop to 15–20% prior to transfusion in otherwise healthy patients undergoing limited excision and transfusing at a hematocrit of 25% in patients with preexisting cardiovascular disease.[209] The same group proposed maintaining hematocrit near 25% in patients with more extensive burns, and near 30% if the patients have preexisting cardiovascular disease. A small study by Sittig and Deitch showed fewer transfused units and no increase in adverse hemodynamic or metabolic effects in patients transfused at a hemoglobin of 6–6.5 g/dL compared to patients maintained at a hemoglobin near 10 g/dL.[210] However, in general, little outcome data exist regarding the optimum transfusion trigger for blood transfusion during burn wound excision. Assessment of blood transfusion needs is best determined by evaluating the clinical status of the patient. Specifically, assessment of ongoing blood losses, preoperative hemoglobin levels, vital signs, and evidence of inadequate oxygen delivery such as hypotension, tachycardia, acidosis, and decreasing mixed venous oxygen tension provide important information regarding the oxygen balance in the patient. In addition, determinations of the patient's oxygen content needs are important in determining the transfusion trigger for an individual patient. Patients with coexisting cardiac and pulmonary disease generally require higher oxygen-carrying capacity. Oxygen requirements will be determined by the type and severity of coexisting conditions. Overall, American Society of Anesthesiologists guidelines indicate that blood transfusion is rarely required at a hemoglobin of 10 g/dL or above and is almost always indicated at a hemoglobin of less than 6 g/dL.[211] For each patient, therefore, acceptable blood loss can be determined based on preexisting diseases, preoperative hematocrit (Hct), and the patients estimated blood volume (EBV). Estimated blood volumes for different patient populations are indicated in Table 14.13.

TABLE 14.13 AVERAGE BLOOD VOLUMES

Age	Blood volume (mL/kg)
Neonate	
Premature	95
Full-term	85
Infants	80
Adults	
Men	75
Women	65

During excision of large burn wounds, patients will often require one or more blood volumes of transfused blood to replace intraoperative blood losses. Massive blood transfusion can be associated with a variety of complications and the use of blood products is associated with significant financial costs.[212]

Several means of decreasing surgical blood loss during burn wound excision may be employed such as the use of tourniquets on limbs and compression dressings at sites of burn wound excision or skin graft harvesting.[213] Tourniquets have been shown to be an effective strategy for decreasing blood loss during burn wound excision.[208] The drawbacks of tourniquet use are that their effectiveness is limited to surgery on the extremities and tourniquets may interfere with the surgical field. Pharmacological interventions that may decrease blood loss include the use of epinephrine-soaked dressings, or topical epinephrine spray to induce local vasoconstriction. Alternatively, subcutaneous tissues may be infiltrated with epinephrine-containing fluids. The use of epinephrine may be associated with tachycardia and hypertension if significant amounts are absorbed into the systemic circulation. However, some studies have reported that the use of topical or subcutaneous epinephrine in burn patients is not associated with an increased incidence of side-effects or complications.[214] However, the effectiveness of this approach is unclear. A recent study showed that the use of topical epinephrine spray or subcutaneous epinephrine infiltration did not result in decreased blood loss during burn wound excision.[215] However, the data were quite variable and the patients also received topical thrombin. A larger study examining the effects of subcutaneous epinephrine and topical thrombin might clarify this issue. In a more recent study, Mzezewa and colleagues reported that treatment with systemic terlipressin, a vasopressin analog, decreased blood loss and transfusion requirements in a cohort of pediatric and adult burn patients[216] The authors did not report significant complications associated with this approach.

Blood components

Several blood components are available for replacement of losses incurred during burn wound excision. These components include:

Whole blood

Whole blood consists of unfractionated blood and contains all of the components of blood including red blood cells, plasma,

platelets, and white blood cells, however, whole blood stored for more than 24 hours does not contain functional white blood cells or platelets (Table 14.14). One unit of whole blood contains approximately 200 mL of red blood cells and 250 mL of plasma. Whole blood is available in some hospitals for large volume blood transfusions (trauma, liver transplantation, burns) and treatment of hypovolemic shock. However, because of the scarcity of blood products in most communities, whole blood is not readily available. Fractionation of whole blood into its individual components is a much more efficient and cost-effective means of maximizing blood usage. When available, however, whole blood provides an excellent means of volume expansion and providing oxygen carrying capacity in patients requiring large volume blood transfusion.

Packed red blood cells

Packed red blood cells (PRBCs) are the most common means of replacing RBC loss during surgical procedures. Most of the plasma and platelets are removed during processing so that PRBCs provide few plasma components, clotting factors, or platelets. A unit of PRBCs contains approximately 200 mL of red cells and 50 mL of residual plasma. A comparison of PRBC composition with whole blood is shown in Table 14.15. PRBCs provide oxygen-carrying capacity and, when reconstituted with crystalloid or plasma, volume resuscitation.

Fresh frozen plasma

In the setting of burn injury, fresh frozen plasma (FFP) is most commonly used to replace clotting factors during massive blood transfusion. FFP will replace clotting factors as well as protein S and protein C by a factor of 2–3% per unit. The initial recommended volume is 10–15 mL/kg. The use of FFP varies among different burn centers. Plasma is frozen within 6 hours of collection and each unit provides approximately 250 mL of plasma containing normal levels of all coagulation factors. A National Institutes of Health consensus conference has recommended usage guidelines for FFP (Table 14.16).

In the setting of massive blood transfusion, FFP administration is indicated if active bleeding exists and laboratory evidence of coagulation factor depletion is shown. A volume of 2–6 units is generally used depending on the severity of the coagulopathy. In some burn centers, PRBCs are reconstituted with FFP on a one-to-one basis. Although this practice has not been shown to be deleterious compared to use of PRBCs reconstituted with crystalloid, there is no evidence that it decreases bleeding complications.[217] However, some practitioners argue that the use of FFP rather than crystalloid to reconstitute PRBCs results in less interstitial edema during the postoperative period and may enhance skin graft survival.

Platelets

Platelets are stored at room temperature to maximize viability. The incidence of bacterial contamination increases exponentially after 4 days. However, refrigerated platelets remain viable for only 24–48 hours. Platelets are obtained from either units of whole blood or by apheresis from a single donor. ABO-compatible platelets, particularly if from a single donor, should be used when possible because post-transfusion viability is improved. One unit of whole blood platelets contains approximately 5×10^{10} platelets in 50 mL of plasma. Most commonly, 6 units of platelets are combined into a single bag and transfused. A unit of single-donor platelets contains about 30×10^{10} platelets suspended in 200–400 mL of plasma. Therefore, 1 unit of single-donor platelets is equal to about 6 units of whole blood platelets. One unit of whole blood platelets will increase the platelet count by 5000–10 000/ L.

TABLE 14.14 CHANGES THAT OCCUR DURING STORAGE OF WHOLE BLOOD IN CITRATE–PHOSPHATE–DEXTROSE

	Days of storage at 4°C			
	1	7	14	21
pH	7.1	7.0	7.0	6.9
PCO_2 (mmHg)	48	80	110	140
Potassium (mEq/L)	3.9	12	17	21
2,3-Diphosphoglycerate (mol/mL)	4.8	1.2	1	1
Viable platelets (%)	10	0	0	0
Factors V and VII (%)	70	50	40	20

TABLE 14.15 COMPARISON OF WHOLE BLOOD AND PACKED RED BLOOD CELLS

Value	Whole blood	Packed red blood cells
Volume (mL)	517	300
Erythrocyte mass (mL)	200	200
Hematocrit (%)	40	70
Albumin (g)	12.5	4
Globulin (g)	6.25	2
Total protein (g)	48.8	36
Plasma sodium (mEq)	45	15
Plasma potassium (mEq)	15	4
Plasma acid (citric/lactic) (mEq)	80	25
Donor/recipient ratio	1 unit per patient	1 unit every 4–6 patients

TABLE 14.16 INDICATIONS FOR FFP ACCORDING TO NATIONAL INSTITUTES OF HEALTH GUIDELINES

A.	Replacement of isolated factor deficiencies (as documented by laboratory evidence)
B.	Reversal of warfarin effect
C.	In antithrombin III deficiency
D.	Treatment of immunodeficiencies
E.	Treatment of thrombotic thrombocytopenia purpura
F.	Massive blood transfusion (only when factors V and VIII are 25% of normal)
G.	Requirements for indications A and F would be a prothrombin and partial thromboplastin time of 1.5 times normal

Cryoprecipitate

Cryoprecipitate is prepared by thawing FFP at 4°C and collecting the precipitate. Cryoprecipitate is rich in factors VIII and XIII, fibrinogen and von Willebrand's factor. In the setting of massive blood transfusion, it is used primarily to treat hypofibrinogenemia. Generally, cryoprecipitate is administered when plasma fibrinogen levels fall below 100 mg/dL. One unit of cryoprecipitate will increase plasma fibrinogen levels by 5–7 mg/dL.

Complications of massive blood transfusion

Coagulopathy

Coagulopathy associated with massive blood transfusion is due to thrombocytopenia or depletion of coagulation factors. PRBCs are essentially devoid of platelets, and whole blood stored for more than 24 hours does not possess significant numbers of viable platelets. Whole blood contains essentially normal levels of coagulation factors with the exception of the volatile factors V and VIII. Because most plasma is removed from PRBCs, they provide a poor source of coagulation factors. Massive blood loss and transfusion with PRBCs or whole blood results in dilutional losses of both platelets and factors V and VIII.

Thrombocytopenia is the most common cause of nonsurgical bleeding after massive blood transfusion. In general, 15–20 units, or 2–4 blood volumes of blood or PRBCs, must be transfused before bleeding due to thrombocytopenia will develop (Figure 14.10). Observed platelet counts usually remain higher than calculated values due to release of platelets from sites of sequestration. Bleeding due to thrombocytopenia usually develops when the platelet count drops below 50–100 000 platelets/ L. Replacement of platelets usually requires transfusion of 6 units of whole blood platelets or 1 unit of single-donor platelets as described earlier in this chapter.

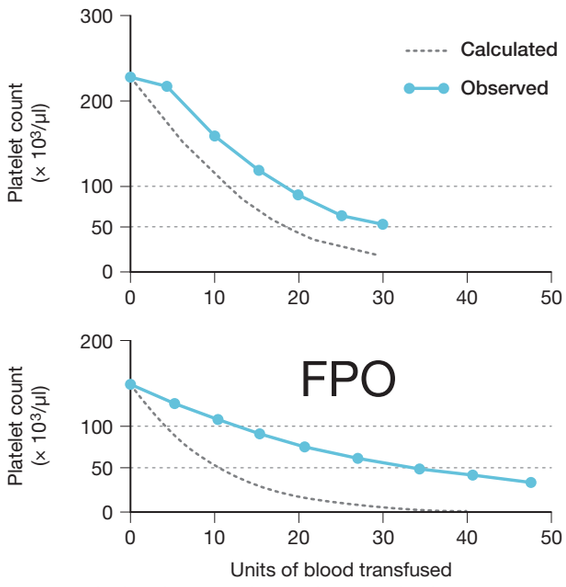


Fig. 14.10 Calculated versus observed mean platelet counts in two studies of platelet count after massive blood transfusion. (From: Reed RL, et al. Prophylactic platelet administration during massive transfusion. Ann Surg 1986; 203:46.)

Development of coagulopathy due to depletion of coagulation factors is also possible during massive blood transfusion. Significant prolongation of the prothrombin (PT) and partial thromboplastin time (PTT) can result after transfusion of 10–12 units of PRBCs. Generally, FFP should be given to correct dilutional coagulopathy if the PT and PTT exceed 1.5 times normal levels. It is also important to know the fibrinogen level in massively transfused patients since hypofibrinogenemia can also result in prolongation of the PT and PTT. Fibrinogen may be replaced using cryoprecipitate.

Citrate toxicity

Citrate is universally used as an anticoagulant in the storage of blood because of its ability to bind calcium that is required for activation of the coagulation cascade. Citrate is metabolized by the liver and excreted by the kidneys. Patients with normal liver and kidney function are able to respond to a large citrate load much better than patients with hepatic or renal insufficiency. During massive blood transfusion, citrate can accumulate in the circulation, resulting in a fall in ionized calcium.[218] Hypocalcemia can result in hypotension, reduced cardiac function, and cardiac arrhythmias. Severe hypocalcemia can also result in clotting abnormalities. However, the level of calcium required for adequate coagulation is much lower than that necessary to maintain cardiovascular stability. Therefore, hypotension and decreased cardiac contractility occur long before coagulation abnormalities are seen. During massive blood transfusion it is generally prudent to monitor ionized calcium, especially if hemodynamic instability is present in the hypocalcemic patient.

Potassium abnormalities

During the storage of whole blood or packed red cells, potassium leaks from erythrocytes into the extracellular fluid and can accumulate at concentrations of 40–80 mEq/L. Once the RBCs are returned to the *in vivo* environment, the potassium quickly reenters RBCs. However, during rapid blood transfusion, transient hyperkalemia may result, particularly in patients with renal insufficiency. The transient hyperkalemia, particularly in the presence of hypocalcemia, can lead to cardiac dysfunction and arrhythmias. In patients with renal insufficiency, potassium load can be minimized by the use of either freshly obtained blood or washed packed RBCs. Hypokalemia can also result from massive blood transfusion due to reentry of potassium into RBCs and other cells during stress, alkalosis, or massive catecholamine release associated with large volume blood loss. Therefore, potassium levels should be monitored routinely during large volume blood transfusions.

Acid-base abnormalities

During the storage of whole blood, an acidic environment develops due to the accumulation of lactate and citrate with a pH in the range of 6.5–6.7. Rapid transfusion of this acidic fluid can contribute to the metabolic acidosis observed during massive blood transfusion. However, metabolic acidosis in this setting is more commonly due to relative tissue hypoxia and anaerobic metabolism due to an imbalance of oxygen con-

sumption and delivery. The anaerobic metabolism that occurs during states of hypovolemia and poor tissue perfusion results in lactic acidosis. Generally, administration of sodium bicarbonate is not indicated. The re-establishment of tissue perfusion and homeostasis is a much more important factor in re-establishing acid-base balance. In contrast, many patients receiving massive blood transfusion will develop a metabolic alkalosis during the post-transfusion phase. This is due to the conversion of citrate to sodium bicarbonate by the liver and is an additional reason to avoid sodium bicarbonate administration during massive blood transfusion except in cases of severe metabolic acidosis (base deficit >12).

Altered oxygen transport

During the storage of blood, red blood cell 2,3-diphosphoglycerate (DPG) levels decline. This results in a shift in the oxyhemoglobin dissociation curve to the left. Under these conditions, oxygen has a higher affinity for hemoglobin, and oxygen release at the tissue level is theoretically diminished. In clinical practice, this alteration in oxygen affinity has not been shown to be functionally significant.

Hypothermia

Rapid infusion of large volumes of cold (4°C) blood can result in significant hypothermia. When added to the already impaired thermoregulatory mechanisms in burn patients this can result in significant hypothermia. Potential complications of hypothermia include altered citrate metabolism, coagulopathy, and cardiac dysfunction. During large volume blood transfusion in burn patients, fluids should be actively warmed with systems designed to effectively warm large volumes of rapidly transfused blood. In addition, the room temperature should be elevated and the patient's extremities and head covered to minimize heat loss. Body temperature should be maintained at or above 37°C in burn patients.

Pulmonary complications

Pulmonary edema is a potential complication of massive blood transfusion. This may result from volume overload and/or pulmonary capillary leak due to inflammation and microaggregates present in transfused blood. Some studies have indicated that the incidence of pulmonary edema is more related to the patient's underlying injury than to blood transfusion per se. However, volume status should be monitored closely during large volume blood transfusion so that volume overload may be avoided.

Transfusion reactions

Hemolytic transfusion reactions are a relatively rare but devastating complication of blood transfusion. The incidence of transfusion reactions is approximately 1:5000 units transfused and fatal transfusion reactions occur at a rate of 1:100 000 units transfused. Most severe reactions result from ABO incompatibility. The most common cause of transfusing ABO-incompatible blood is clerical error. Therefore, most hospitals have developed policies that require multiple checks of the blood prior to transfusion. A list of blood types and associated circulating antibodies is shown in Table 14.17. Massive hemolytic transfusion reactions result from destruction of transfused erythrocytes by circulating antibodies and complement. Many of the common signs and symptoms of transfusion reactions (Table 14.18), such as chills, chest pain, and nausea, cannot be detected in the patient under anesthesia. The most commonly recognized signs of transfusion reaction in the anesthetized patient are fever, hypotension, hemoglobinuria, and coagulopathy. The steps involved in the treatment of hemolytic transfusion reaction are outlined in Table 14.19. The cornerstones of treatment are to stop the transfusion, protect the kidneys with aggressive hydration and alkalinization of urine, and treat existing coagulopathy.

Delayed hemolytic transfusion reactions can occur in patients that have received prior blood transfusions and result from a secondary immune response with production of antibodies to blood antigens. This reaction can occur from 2 to 21 days after transfusion and should be suspected in patients with unexplained decreases in hematocrit during the postoperative

TABLE 14.18 FREQUENCY AND SIGNS AND SYMPTOMS FROM HEMOLYTIC TRANSFUSION REACTIONS IN 40 PATIENTS

Sign or symptom	No. of patients
Fever	19
Fever and chills	16
Chest pain	6
Hypotension	6
Nausea	2
Flushing	2
Dyspnea	2
Hemogloburia	1

TABLE 14.17 BLOOD GROUPS AND CROSS-MATCH

Blood group	Antigen on erythrocyte	Plasma antibodies	Incidence (%) Whites	African-* Americans
A	A	Anti-B	.40	27
B	B	Anti-A	11	20
AB	AB	None	4	4
O	None	Anti-A Anti-B	45	49
Rh	Rh		42	17

TABLE 14.19 STEPS FOR THE TREATMENT OF A HEMOLYTIC TRANSFUSION REACTION

1.	STOP THE TRANSFUSION
2.	Maintain the urine output at a minimum of 75–100 mL/h by the following methods:
a.	Generously administer fluids intravenously and possibly mannitol, 12.5–50 g, given over a 5 to 15-minute period
b.	If intravenously administered fluids and mannitol are ineffective, then administer furosemide, 20–40 mg, IV
3.	Alkalinize the urine; since bicarbonate is preferentially excreted in the urine, only 40–70 mEq/70 kg of sodium bicarbonate is usually required to raise the urine pH to 8, whereupon repeat urine pH determinations indicate the need for additional bicarbonate
4.	Assay urine and plasma hemoglobin concentrations
5.	Determine platelet count, partial thromboplastin time, and serum fibrinogen level
6.	Return unused blood to blood bank for re-cross-match
7.	Send patient blood sample to blood bank for antibody screen and direct antiglobulin test
8.	Prevent hypotension to ensure adequate renal blood flow

period. Renal injury is less common than in acute hemolytic reactions but adequate hydration and alkalinization of urine are usually indicated. Febrile reactions are common following blood transfusion and are generally due to contaminating leukocytes and leukocyte antigens present in transfused blood. Pure febrile reactions usually do not require termination of the transfusion but the patient should be monitored closely to assure that a more severe transfusion reaction is not developing.

Infection

Infection is a major problem in burn patients due to disruption of the cutaneous barrier and immunosuppression. Blood transfusion adds to the infection risk. Graves and colleagues showed a significant correlation between the number of blood transfusions and infectious complications in burn patients.[219] The most common source of major infection from blood products is hepatitis. Hepatitis C is the most common offender, followed by hepatitis B. The incidence of hepatitis C is approximately 3 in 10 000 units transfused. The development of rigorous screening mechanisms has markedly decreased the incidence of HIV infection to 1 in 200 000–500 000 units transfused. Cytomegalovirus (CMV) has been identified in blood products and could cause clinically significant problems in immunocompromised burn patients. However, the incidence of clinically important CMV infection is low in burn patients.

Postoperative care

Decisions regarding postoperative airway management and support of ventilation depend on several factors. Extubation is desirable as soon as it is indicated but in burn patients for a number of reasons it often it may be even more important not to extubate when it is not indicated. If the patient came to the operating room intubated the indication for intubation must

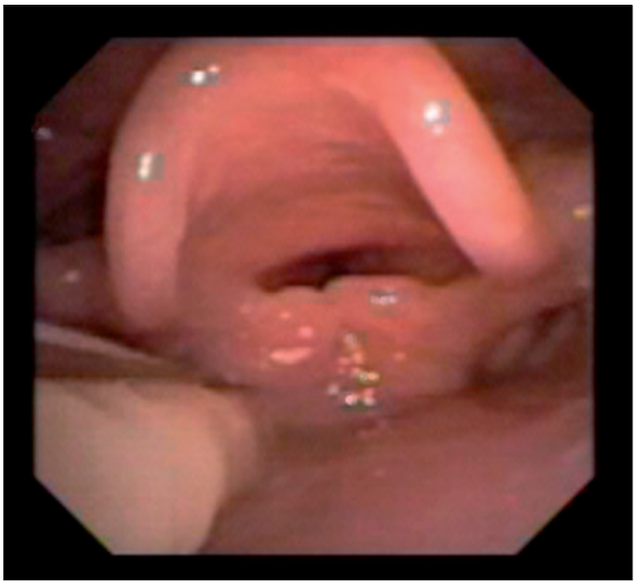


Fig. 14.11 Inflammation of the larynx caused by thermal, mechanical, or chemical irritation may result in swelling of the mucosa over the arytenoids emminance and this redundant tissue can fold into the glottic inlet and cause obstruction.

be determined. If the initial indication has resolved the decision to extubate depends on perioperative events. Some patients with neck and facial burns are intubated to protect the airway from obstruction by edema. The airway must be examined to be sure edematous tissues will not cause obstruction when the endotracheal tube is removed. Air leaking around a deflated endotracheal tube cuff during positive pressure ventilation is an encouraging sign that the airway may remain patent after extubation. The upper airway can also be examined by direct laryngoscopy or with an endoscope. In marginal cases the endotracheal tube can be removed while an exchanger is left in the trachea. Another technique is to extubate under direct vision with a bronchoscope with an endotracheal tube already loaded on the bronchoscope. Especially in small pediatric patients a common reason for post extubation stridor and failed extubation is edematous and redundant mucosa over the arytenoid eminences that obstruct the glottic inlet during inspiration (Figure 14.11). This condition can be exacerbated by an endotracheal tube that is too large, excessive patient motion due to inadequate sedation and analgesia, reflux of acidic gastric contents, and mechanical irritation due to compression of the posterior laryngeal structures between the endotracheal tube and gastric tubes. These irritants can also cause laryngomalacia in pediatric patients (Figure 14.12). If laryngeal obstruction persists despite attention to all these details a short course of steroids is often effective as long as concerns regarding burn wound infection do not preclude the use of steroids (unpublished observations.) Heliox has also been used successfully in this situation.[220]

After transfer of monitors and ventilatory support in the intensive care unit, a full report of the intraoperative anesthetic course is given, along with information about the patient's current condition and therapy. A chest radiograph

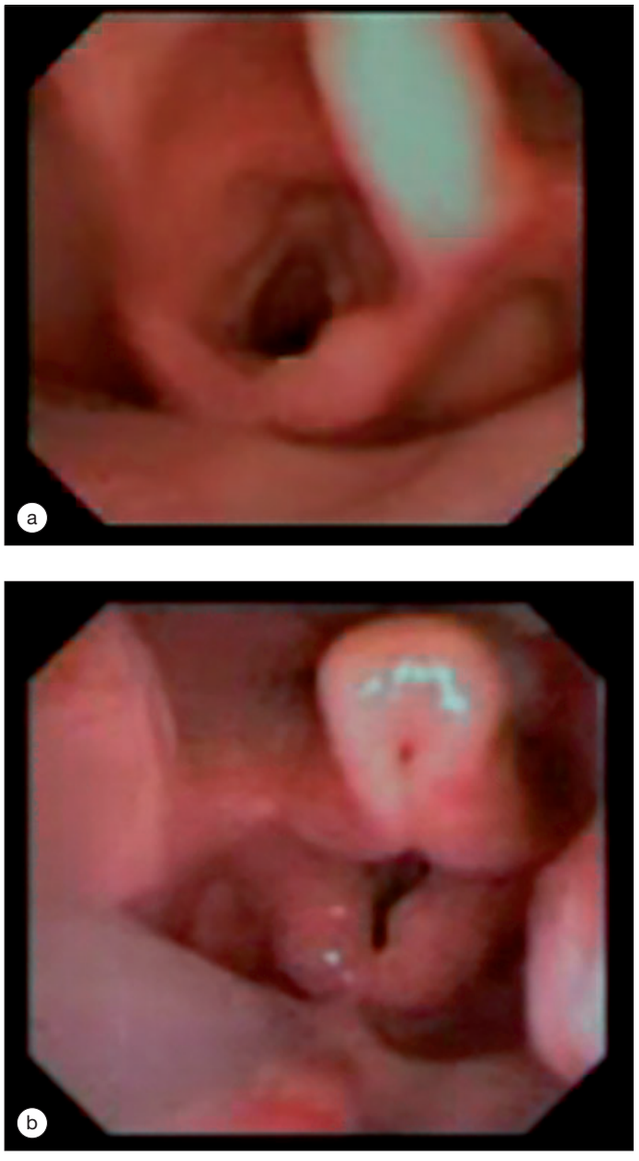


Fig. 14.12 Laryngomalacia due to local irritation and inflammation can cause dynamic inspiratory airway obstruction. (a) During exhalation the glottic opening is patent but (b)during inhalation the larynx collapses and obstructs air flow.

may be needed for vascular catheters placed in the OR or to check position of an endotracheal tube if the patient will be ventilated postoperatively. Laboratory studies including arterial blood gas, blood chemistries, renal function tests, hematocrit, platelet count, and coagulation studies are sent soon after patient arrival to the intensive care unit. These studies are particularly important if massive transfusion was required in the operating room.

One of the most important issues in the immediate postoperative period for burn patients is adequate analgesia and sedation, particularly for the intubated and mechanically ventilated patient. Debridement of burned tissue and the harvesting of skin grafts are painful procedures that merit ample analgesic doses in order to insure patient comfort. It is not uncommon for burn patients to be quite tolerant to narcotic analgesics, especially after they have had several operative procedures, and in this case larger doses than normal are required.

Ongoing blood loss is unfortunately a common problem after the excision and grafting of a large burn wound, even when strict attention is placed on intraoperative hemostasis by surgical personnel. The burn wounds are necessarily excised down to bleeding tissue before skin grafts are applied. Massive intraoperative transfusion adds to the problem with dilutional thrombocytopenia and coagulopathy. Diligent postoperative care is needed to continually assess ongoing blood loss and transfuse additional blood products as they are indicated by clinical course and laboratory studies. Ongoing bleeding may manifest as hypovolemia and hypotension even in the brief period of transport from the operating room to the intensive care unit. Monitoring of central venous pressure and urine output also help in guiding postoperative blood and fluid therapy.

Adequate ventilation is essential in the postoperative period in order to minimize hypoxemia and hypercarbia. Blood gases and oxygen saturation can be used as guides to ventilator management. Patients with inhalation injury benefit not only from rational ventilator management but also from a program of inhaled bronchodilators and mucolytics combined with judicious airway suctioning. Extubated patients require supplemental oxygen for at least the first few hours postoperatively in order to maintain adequate oxygen saturation. Airway support may also be necessary initially in these patients until they are more alert and responsive.

Finally, burn patients must be recovered in a warm environment. Postoperative hypothermia can result in vasoconstriction, hypoperfusion, and metabolic acidosis. Radiant heaters, blood and fluid warmers, warm blankets, heated humidifiers for gas delivery, and high room temperature are all useful in the postoperative period to provide warmth to the recovering patient.

Summary

Anesthetic management of the burn patient presents numerous challenges. Anatomical distortions make airway management and vascular access difficult. Pathophysiological changes in cardiovascular function range from initial hypovolemia and impaired perfusion to a hyperdynamic and hypermetabolic state that develops after the resuscitative stage. These and other changes profoundly alter response to anesthetic drugs. Effective anesthetic management will depend on knowledge of the continuum of pathophysiological changes, technical skills, proper planning, and availability of proper resources. A team approach is necessary, keeping in mind that perioperative management should be compatible with ICU management and goals. This requires close communication with other members of the burn care team and is one of the most important principles of effective anesthetic management of these challenging patients.

References

1. Saffle VR. Predicting outcomes of burns. N Engl J Med 1998; 338:387–388.
2. Ryan CM, Schoenfeld DA, Thorpe WP, et al. Objective estimates of the probability of death from burn injuries. N Engl J Med 1998; 338:362–366.
3. O'Keefe GE, Hunt JL, Purdue GF. An evaluation of risk factors for mortality after burn trauma and the identification of gender-dependent differences in outcomes. J Am Coll Surg 2001; 192:153–160.
4. Sheridan RL, Remensnyder JP, Schnitzer JJ, et al. Current expectations for survival in pediatric burns. Arch Pediatr Adolesc Med 2000; 154(3):245–249.
5. MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. Anesthesiology 1998; 89:749–770.
6. Beushausen T, Mucke ••. Anesthesia and pain management in pediatric burn patients. Pediatric Surg Int 1997; 12:327–333.
7. Martyn JAJ ed. Acute management of the burned patient. London: WB Saunders; 1990.
8. Woodson LC, Sherwood ER, Cortiella J, et al. Anesthesia for reconstructive burn surgery. In: McCauley ••, Taylor ••, Francis ••, eds. Functional and aesthetic reconstruction of burned patients. •• 2005:85–103.
9. Reynolds EM, Ryan DP, Sheridan RL, et al. Left ventricular failure complicating severe pediatric burn injuries. J Pediatric Surg 1995; 30:264–269.
10. Desai MH, Herndon DN, Broemeling L, et al. Early burn wound excision significantly reduces blood loss. Ann Surg 1990; 211:753–759.
11. Thompson PB, Herndon DN, Traber DL, et al. Effect on mortality of inhalation injury. J Trauma 1986; 26:163–165.
12. Navar PD, Saffle JR, Warden GD. Effect of inhalation injury on fluid resuscitation requirements after thermal injury. Am J Surg 1985; 150:716–720.
13. Hollingsed TC, Saffle JR, Barton RG, et al. Etiology and consequences of respiratory failure in thermally injured patients. Am J Surg 1993; 166:592–597.
14. Foley FD. The burn autopsy. Am J Clin Pathol 1969; 52:1–13.
15. Moritz AR, Henriques FC, McLean R. The effects of inhaled heat on the air passages and lungs: an experimental investigation. Am J Pathol 1945; 21:311–331.
16. Clark WR, Bonaventura M, Myers W. Smoke inhalation and airway management at a regional burn unit: 1974–1983. Diagnosis and consequences of smoke inhalation. J Burn Care Rehabil 1989; 10:52–62.
17. Muehlberger T, Kunar D, Munster A, et al. Efficacy of fiberoptic laryngoscopy in the diagnosis of inhalation injuries. Arch Otolaryngol Head Neck Surg 1998; 124:1003–1007.
18. Colice GL, Munster AM, Haponik EF. Tracheal stenosis complicating cutaneous burns: an underestimated problem. Am Rev Respir Dis 1986; 134:1315–1318.
19. Clark CJ, Reid WH, Telfer ABM, et al. Respiratory injury in the burned patient; the role of flexible bronchoscopy. Anaesthesia 1983; 38:35–39.
20. Haponic EF, Lykens MG. Acute upper airway obstruction in patients with burns. Crit Care Rep 1990; 2:28–49.
21. Hunt JL, Agee RN, Pruitt BA. Fiberoptic bronchoscopy in acute inhalation injury. J Trauma 1975; 15:641–649.
22. Haponic EF, Myers DA, Munster AM, et al. Acute upper airway injury in burn patients: serial changes of flow-volume curves and nasopharyngoscopy. Am Rev Respir Dis 1987; 135:360–366.
23. Lee JM, O'Connell DJ. The plain chest radiograph after acute smoke inhalation. Clin Radiol 1988; 39:33.
24. Linares HA, Herndon DN, Traber DL. Sequence of morphologic events in experimental smoke inhalation. J Burn Care Rehabil 1989; 10:27–37.
25. Demling RH, Chen C. Pulmonary function in the burn patient. Semin Nephrol 1993; 13:371–81.
26. Sheridan RL, Kacmarek RM, McEttrick MM, et al. Permissive hypercapnia as a ventilatory strategy in burned children: effect on barotrauma, pneumonia and mortality. J Trauma 1995; 39(5):854–859.
27. Cioffi WG Jr, Rue LW III, Graves TA, et al. Prophylactic use of high-frequency percussive ventilation in patients with inhalation injury. Ann Surg 1991; 213(6):575–580; discussion 580–582.
28. Fitzpatrick JC, Cioffi WG, Jr. Ventilatory support following burns and smoke-inhalation injury. Respir Care Clin N Am 1997; 3(1):21–49.
29. Reper P, Dankaert R, van Hille F, et al. The usefulness of combined high-frequency percussive ventilation during acute respiratory failure after smoke inhalation. Burns 1998; 24(1):34–38.
30. Cortiella J, Mlcak R, Herndon DN. High frequency percussive ventilation in pediatric patients with inhalation injury. J Burn Care Rehabil 1999; 20(3):232–235.
31. Ernst A, Zibrak JD. Carbon monoxide poisoning. N Engl J Med 1998; 339:1603–1608.
32. Tibbles P, Perrotta P. Treatment of carbon monoxide poisoning: a critical review of human outcome studies comparing normobaric oxygen with hyperbaric oxygen. Ann Emerg Med 1994; 24:269–276.
33. Clark CJ. Measurement of toxic combustion products in fire survivors. J Roy Soc Med 1982; 153:41–44.
34. Cummings TE. The treatment of cyanide poisoning. Occupational Medicine 2004; 54:82–85.
35. Hardman JG, Limbird LE, Goodman Gilman A. Goodman and Gilman's-The pharmacological basis or therapeutics. 10th edn. ••: Pergamon; 2001:1892–1893.
36. Deitch EA. The management of burns. N Engl J Med 1990; 323:1249–1253.
37. Horton JW, Baxter CR, White DJ. Differences in cardiac responses to resuscitation from burn shock. Surg Gynecol Obstet 1989; 168:201–213.
38. Zetterstrom H, Arturson G. Plasma oncotic pressure and plasma protein concentration in patients following thermal injury. Acta Anaesthesiol Scand 1980; 24:288–294.
39. Kinsky MP, Guha SC, Button BM, et al. The role of interstitial Starling forces in the pathogenesis of burn edema. J Burn Care Rehabil 1998; 19(1 Pt 1):1–9.
40. Baxter CR, Cook WA, Shires GT. Serum myocardial depressant factor of burn shock. Surg Forum 1966; 17:1–2.
41. Maass DL, White J, Horton JW. IL-1beta and IL-6 act synergistically with TNF-alpha to alter cardiac contractile function after burn trauma. Shock 2002; 18(4):360–366.
42. Horton JW, Tan J, White DJ, et al. Selective decontamination of the digestive tract attenuated the myocardial inflammation and dysfunction that occur with burn injury. Am J Physiol Heart Circ Physiol 2004; 287(5):H2241–H2251.
43. Horton JW. Left ventricular contractile dysfunction as a complication of thermal injury. Shock 2004; 22(6):495–507. Review.
44. Westphal M, Noshima S, Isago T, et al. Selective thromboxane A2 synthase inhibition by OKY-046 prevents cardiopulmonary dysfunction after ovine smoke inhalation injury Anesthesiology 2005; 102(5):954–961.
45. Muller-Werdan U, Engelmann H. Werdan K. Cardiodepression by tumor necrosis factor-alpha. Eur Cytokine Netw 1998; 9:689–691.
46. Roberts AB, Vodovotz Y, Roche NS, et al. Role of nitric oxide in antagonistic effects of transforming growth factor-beta and interleukin-1 beta on the beating rate of cultured cardiac myocytes. Mol Endocrinol 1992; 6:1921–1930.
47. Cartotto RC, Innes M, Musgrave MA, et al. How well does the Parkland formula estimate actual fluid resuscitation volumes? J Burn Care Rehabil 2002; 23(4):258–265.
48. Alderson P, Schierhout G, Roberts I, et al. Colloids versus crystalloids for fluid resuscitation in critically ill patients. Cochrane Database Syst Rev 2000; 2:CD000567.
49. Nguyen TT, Gilpin DA, Meyer NA, et al. Current treatment of severely burned patients. Ann Surg 1996; 223:14–25.

50. Alderson P, Bunn F, Lefebvre C, et al. The albumin reviewers. Human albumin solution for resuscitation and volume expansion in critically ill patients. Cochrane Database Syst Rev 2000; 2: CD001208.
51. O'Mara MS, Slater H, Goldfarb IW, et al. A prospective, randomized evaluation of intra-abdominal pressures with crystalloid and colloid resuscitation in burn patients. J Trauma 2005; 58(5):1011–1018.
52. Guha SC, Kinsky MP, Button B, et al. Burn resuscitation: crystalloid versus colloid versus hypertonic saline hyperoncotic colloid in sheep. Crit Care Med 1996; 24:1849–1857.
53. Elgjo Gl, Poli de Figueiredo LF, et al. Hypertonic saline dextran produces early (8–12 hours) fluid sparing in burn resuscitation: a 24-hour prospective, double-blind study in sheep. Crit Care Med 2000; 28:163–171.
54. Suzuki K, Ogino R, Nishina M, et al. Effects of hypertonic saline and dextran cardiac functions after burns. Am J Physiol 1995; 268(2 Pt 2):H856–H864.
55. Jeng JC, Lee K, Jablonski K, et al. Serum lactate and base deficit suggest inadequate resuscitation of patients with burn injuries: application of a point-of-care laboratory instrument. J Burn Care Rehabil 1997; 18:402–405.
56. Dries DJ, Waxman K. Adequate resuscitation of burn patients may not be measured by urine output and vital signs. Crit Care Med 1991; 19:327–329.
57. Wo CC, Shoemaker WC, Appel PL, et al. Unreliability of blood pressure and heart rate to evaluate cardiac output in emergency resuscitation and critical illness. Crit Care Med 1993; 21:218–223.
58. Schiller WR, Bay RC, Garren RL, et al. Hyperdynamic resuscitation improves survival in patients with life-threatening burns. J Burn Care Rehabil 1997; 18:10–16.
59. Holm C, Melcer B, Horbrand F, et al. The relationship between oxygen delivery and oxygen consumption during fluid resuscitation of burn-related shock. J Burn Care Rehabil 2000; 21:147–154.
60. Bernard F, Gueugniaud PY, Bertin-Maghit M, et al. Prognostic significance of early cardiac index measurements in severely burned patients. Burns 1994; 20:529–531.
61. Bishop MH, Shoemaker WC, Appel PL, et al. Prospective, randomized trial of survivor values of cardiac index, oxygen delivery, and oxygen consumption as resuscitation endpoints in severe trauma. J Trauma 1995; 38:780–787.
62. Fleming A, Bishop M, Shoemaker W, et al. Prospective trial of supranormal values as goals of resuscitation in severe trauma. Arch Surg 1992; 127:1175–1179.
63. Schiller WR, Bay RC, Garren RL, et al. Hyperdynamic resuscitation improves survival in patients with life-threatening burns. J Burn Care Rehabil 1997; 18:10–16.
64. Heyland DK, Cook DJ, King D, et al. Maximizing oxygen delivery in critically ill patients: a methodologic appraisal of the evidence. Crit Care Med 1996; 24:517–524.
65. Gattinoni L, Brazzi L, Pelosi P, et al. A trial of goal-oriented hemodynamic therapy in critically ill patients. SvO2 Collaborative Group. N Engl J Med 1995; 333:1025–1032.
66. Durham RM, Neunaber K, Mazuski JE, et al. The use of oxygen consumption and delivery as endpoints for resuscitation in critically ill patients. J Trauma 1996; 41:32–39.
67. Hayes MA, Timmins AC, Yau EH, et al. Elevation of systemic oxygen delivery in the treatment of critically ill patients. N Engl J Med 1994; 330:1717–1722.
68. Hendenstierna G. What value does the recording of intrathoracic blood volume have in clinical practice? Intensive Care Med 1992; 18(3):142–147.
69. Kuntscher MV, Czermak C, Blome-Eberwein S, et al. Transcardiopulmonary thermal dye versus single thermodilution methods for assessment of intrathoracic blood volume and extravascular lung water in major burn resuscitation. J Burn Care Rehabil 2003; 24:142–147.
70. Holm C, Melcer B, Horbrand F, et al. Intrathoracic blood volume as an end point in resuscitation of the severely burned: an observational study of 24 patients. J Trauma 2000; 48(4):728–734.
71. Porter JM, lvatury RR. In search of the optimal end points of resuscitation in trauma patients: a review. J Trauma 1998; 44:908–914.
72. Holm C, Melcer B, Horbrand F, et al. Haemodynamic and oxygen transport responses in survivors and non-survivors following thermal injury. Burns 2000; 26:25–33.
73. Kaups KL, Davis JW, Dominic WJ. Base deficit as an indicator or resuscitation needs in patients with burn injuries. J Burn Care Rehabil 1998; 19:346–348.
74. Robbins MR, Smith RS, Helmer SD. Serial pHi measurement as a predictor of mortality, organ failure, and hospital stay in surgical patients. Am Surg 1999; 65:715–719.
75. Engrav LV, Colescott PL, Kemalyan N, et al. A biopsy of the use of the Baxter formula to resuscitate burns or do we do it like Charlie did it? J Burn Care Rehabil 2000; 21(2):91–95.
76. Pirson J, Zizi M, Jacob E, et al. Acute ischemic optic neuropathy associated with and abdominal compartment syndrome in a burn patient. Burns 2004; 30:491–494.
77. Greenhalgh DG, Warden GD. The importance of intra-abdominal pressure measurements in burned children. J Trauma 1994; 36(5):685–690.
78. Ivy ME, Atweh NA, Palmer J, et al. Intra-abdominal hypertension and abdominal compartment syndrome in burn patients. J Trauma 2000; 49(3):387–391.
79. Ivatury RR, Sugerman HJ, Peitzman AB. Abdominal compartment syndrome: recognition and management. Advances in Surgery 2001; 35:251–269.
80. Oda J, Ueyama M, Yamashita K, et al. Effects of escharotomy as abdominal decompression on cardiopulmonary function and visceral perfusion in abdominal compartment syndrome with burn patients. J Trauma 2005; 59(2):368–373.
81. Corcos AC, Sherman HF. Percutaneous treatment of secondary abdominal compartment syndrome. J Trauma 2001; 51(6): 1062–1064.
82. Santos AP, Wilson AK, Hornung CA, et al. Methamphetamine laboratory explosions: a new and emerging burn injury. J Burn Care Rehabil 2005; 26(3):228–232.
83. Warner P, Connolly JP, Gibran NS, et al. The methamphetamine burn patient. J Burn Care Rehabil 2003; 24(5):275–278.
84. Danks RR, Wibbenmeyer LA, Faucher LD, et al. Methamphetamine-associated burn injuries: a retrospective analysis. J Burn Care Rehabil 2004; 25(5):425–429.
85. Mitka M. Meth lab fires put heat on burn centers. JAMA 2005; 294(16):2009–20010.
86. Cooper D, Souther L, Hanlon D, et al. Public health consequences among first responders to emergency events associated with illicit methamphetamine laboratories-selected states, 1996–1999. JAMA 2000; 284(21):2715–2716.
87. Davies MP, Evans J, McGonigle RJ. The dialysis debate: acute renal failure in burns patients. Burns 1994; 20:71–73.
88. Davies DM, Pusey CD, Rainford DJ, et al. Acute renal failure in burns. Scand J Plast Reconstr Surg 1979; 13:189–192.
89. Cameron JS. Disturbances of renal function in burnt patients. Proc R Soc Med 1969; 62:49–50.
90. Kim GH, Oh KH, Yoon JW, et al. Impact of burn size and initial serum albumin level on acute renal failure occurring in major burn. Am J Nephrology 2003; 23:55–60.
91. Jeschke MG, Barrow RE, Wolf SE, et al. Mortality in burned children with acute renal failure. Arch Surg 1998; 133:752–756.
92. Holm C, Horbrand F, von Donnersmarck GH, et al. Acute renal failure in severely burned patients. Burns 1999; 25:171–178.
93. Chrysopoulo MT, Jeschke MG, Dziewulski P, et al. Acute renal dysfunction in severely burned adults. J Trauma 1999; 46:141–144.
94. Herndon DN, Tompkins RG. Support of the metabolic response to burn injury. Lancet. 2004; 363(9424):1895902.
95. Wolfe RR. Herman award lecture, 1996: relation of metabolic studies to clinical nutrition–the example of burn injury. Am J Clin Nutr 1996; 64(5):800–808.
96. Wilmore DW, Long JM, Mason AD, Jr, et al. Catecholamines: mediator of the hypermetabolic response to thermal injury. Ann Surg 1974; 180(4):653–669.

97. Hart DW, Wolf SE, Chinkes DL, et al. Effects of early excision and aggressive enteral feeding on hypermetabolism, catabolism, and sepsis after severe burn. J Trauma 2003; 54(4):755–761, discussion 761–764.
98. Liusuwan RA, Palmieri TL, Kinoshita L, et al. Comparison of measured resting energy expenditure versus predictive equations in pediatric burn patients. J Burn Care Rehabil 2005; 26(6):464–4670.
99. Andel D, Kamolz LP, Donner A, et al. Impact of intraoperative duodenal feeding on the oxygen balance of the splanchnic region in severely burned patients. Burns 2005; 31(3):302–305. Epub 2005 Jan 21.
100. Hart DW, Wolf SE, Chinkes DL, et al. Determinants of skeletal muscle catabolism after severe burn. Ann Surg 2000; 232(4):455–465.
101. Barrow RE, Hawkins HK, Aarsland A, et al. Identification of factors contributing to hepatomegaly in severely burned children. Shock 2005; 24(6):523–528.
102. Langouche L, Van den Berghe G. Glucose metabolism and insulin therapy. Crit Care Clin 2006; 22(1):119–129, vii.
103. Pham TN, Warren AJ, Phan HH, et al. Impact of tight glycemic control in severely burned children. J Trauma 2005; 59(5):1148–1154.
104. Ouattara A, Lecomte P, Le Manach Y, et al. Poor intraoperative blood glucose control is associated with a worsened hospital outcome after cardiac surgery in diabetic patients. Anesthesiology 2005; 103(4):687–694.
105. Sessler DI. Perioperative heat balance. Anesthesiology 2000; 92:578–616.
106. Wallace BH, Caldwell FT Jr, Cone JB. The interrelationships between wound management, thermal stress, energy metabolism, and temperature profiles of patients with burns. J Burn Care Rehabil 1994; 15:499–508.
107. Caldwell FT Jr, Wallace BH, Cone JB. The effect of wound management on the interaction of burn size, heat production, and rectal temperature. J Burn Care Rehabil 1994; 15:121–129.
108. Caldwell FT, Jr, Graves DB, Wallace BH. Pathogenesis of fever in a rat burn model: the role of cytokines and lipopolysaccharide. J Burn Care Rehabil 1997; 18:525–530.
109. Caldwell FT Jr, Graves DB, Wallace BH. Chronic indomethacin administration blocks increased body temperature after burn injury in rats. J Burn Care Rehabil 1998; 19:501–511.
110. Shiozaki T, Kishikawa M, Hiraide A, et al. Recovery from postoperative hypothermia predicts survival in extensively burned patients. Am J Surg 1993; 165:326–330.
111. Pereira CT, Muphy KD, Herndon DN. Altering metabolism. J Burn Care Rehabil 2005; 26:194–199.
112. Zawacki BE, Spitzer KW, Mason AD, et al. Does increased evaporative loss cause hypermetabolism in burned patients? Ann Surg 1970; 171:236–240.
113. Vanni SMA, Braz JRC, Modolo NSP, et al. Preoperative combined with intraoperative skin surface warming avoids hypothermia caused by general anesthesia and surgery. J Clin Anesthesia 2003, 15:119–125.
114. Jaehde U, Sorgel F. Clinical pharmacokinetics in patients with burns. Clin Pharmacokinet 1995; 29:15–28.
115. Bonate PL. Pathophysiology and pharmacokinetics following burn injury. Clin Pharmacokinet 1990; 18:118–130.
116. Martyn JA, Abernethy DR, Greenblatt DJ. Plasma protein binding of drugs after severe burn injury. Clin Pharmacol Ther 1984; 35:535–539.
117. Blaschke TF. Protein binding and kinetics of drugs in liver disease. Clin Pharmacokinet 1977; 2:32–44.
118. Loirat P, Rohan J, Baillet A, et al. Increased glomerulofiltration rate in patients with major burns and its effect on the pharmacokinetics of tobramycin. N Engl J Med 1978; 299: 915–919.
119. Glew RH, Moellering RC, Burke JF. Fentamicin dosage in children with extensive burns. J Trauma 1976; 16:819–823.
120. Perry S, Inturrisi CE. Analgesia and morphine disposition in burn patients. J Burn Care Rehabil 1983; 4:276–279.
121. Furman WR, Munster AM, Cane EJ. Morphine pharmacokinetics during anesthesia and surgery in patients with burns. J Burn Care Rehabil 1990; 11:391–394.
122. Moncrief JA. Complications of burns. Ann Surg 1958; 147:443–475.
123. Tolmie JD, Joyce TH, Mitchell GD. Succinylcholine danger in the burned patient. Anesthesiology 1967; 18:467–470.
124. Schaner PJ, Brown RL, Kirksey TD, et al. Succinylcholine-induced hyperkalemia in burned patients. Anesth Analg 1969; 48:764–770.
125. Martyn JAJ, Szyfelbein SK, Ali HA, et al. Increased d-tubocurarine requirement following major thermal injury. Anesthesiology 1980; 52:352–355.
126. Martyn JAJ, Liu LMO, Szyfelbein SK, et al. The neuromuscular effects of pancuronium in burned children. Anesthesiology 1983; 59:561–564.
127. Martyn JA, Matteo RS, Szfelbein SK, et al. Unprecedented resistance to neuromuscular blocking effects of metocurine with persistence after complete recovery in a burned patient. Anesth Analg 1982; 61:614–617.
128. Kim C, Fuke N, Martyn JA. Burn injury to rat increases nicotinic acetylcholine receptors in the diaphragm. Anesthesiology 1988; 68:401–406.
129. Martyn JA, White DA, Gronert GA, et al. Up- and -down regulation of skeletal muscle acetylcholine receptors. Effects on neuromuscular blockers. Anesth 1992; 76(5):822–843.
130. Martyn JAJ, Richtsfeld M. Succinylcholine-induced hyperkalemia in acquired pathologic states. Anesth 2006; 104(1):158–169.
131. Viby-Mogensen J, Hanel HK, Hansen E, et al. Serum cholinesterase activity in burned patients. II: Anaesthesia, suxamethonium and hyperkalaemia. Acta Anaesthesiol Scand 1975; 19:169–179.
132. McCaughey TJ. Hazards of anesthesia for the burned child. Can Anaesth Soc J 1962; 9:220–233.
133. Yentis SM. Suxamethonium and hyperkalemia. Anaesth Intensive Care 1990; 18:92–101.
134. Gronert GA. Letter to the editor: Succinylcholine hyperkalemia after burns. Anesthesiology 1999; 91:320.
135. MacLenna N, Heimbach DM, Cullen BF. Letter to the editor: Succinylcholine hyperkalemia after burns. Anesthesiology 1999; 91:320.
136. Martyn JA. Letter to editor in reply to: Succinylcholine hyperkalemia after burns. Anesthesiology 1999; 91:321–322.
137. Brown TCK, Bell B. Electromyographic responses to small doses of suxamethonium in children after burns. Br J Anaesth 1987; 59:1017–1021.
138. Han TY, Kim HS, Bae JY, et al. Neuromuscular pharmacodynamics of rocuronium in patients with major burns. Anesth Analg 2004; 99:386–392.
139. Viby-Mogensen J, Hanel HK, Hansen E, et al. Serum cholinesterase activity in burned patients I: biochemical findings. Acta Anaesth Scand 1975; 19:159–163.
140. Martyn JAJ, Chang Y, Goudsouzian NG, et al. Pharmacodynamics of mivacurium chloride in 13 to 18 year old adolescents with thermal injury. Br J Anaesth 2002; 89(4):580–585.
141. Hu OY, Ho ST, Wang JJ, et al. Evaluation of gastric emptying in severe, burn-injured patients. Crit Care Med 1993; 21:527–531.
142. M, Esch O, Lang J, Herbert ME, et al. Magnetic resonance imaging of the upper airway: Effects of propofol anesthesia and nasal continuous positive airway pressure in humans. Anesthesiology 1996; 84:275–278.
143. Lang J, Herbert M, Esch ••, et al. Magnetic resonance of the upper airway: Ketamine preserves airway potency compared to propofol anesthesia in human volunteers. Anesth Anal 1997; 84:542.
144. Wilson RD, Nichols RJ, McCoy NR. Dissociative anesthesia with CI-581 in burned children. Anesth Analg 1967; 46:719–724.
145. Alfery DD, Ward CF, Harwood IR, et al. Airway management for a neonate with congenital fusion of the jaws. Anesthesia 1979; 51:340–342.
146. Kleeman PP, Jantzen JP, Bonfils P. Clinical reports: The ultra-thin bronchoscope in management of the difficult paediatric airway. Can J Anaesth 1987; 34:606–608.

147. Wrigley SR, Black AE, Sidhu VS. A fiberoptic laryngoscope for paediatric anaesthesia; a study to evaluate the use of the 2.2mm Olympus (LF-P) intubating fiberscope. Anaesthesia 1995; 50:709–712.
148. Gordon MD, ed. Burn care protocols: anchoring endotracheal tubes on patients with facial burns. J Burn Care Rehabil 1987; 8:233–237.
149. McCall VE, Fischer CG, Schomaker E, et al. Laryngeal mask airway use in children with acute burns: intraoperative airway management. Paediatr Anaesth 1999; 9:515–520.
150. Hagberg CA, Johnson S, Deepak P. Effective use of the esophageal tracheal Combitube™ following severe burn injury. J Clin Anesth ••; 15:463–466.
151. Sheridan RL, Prelack KM, Petras LM, et al. Intraoperative reflectance oximetry in burn patients. J Clin Monit 1995; 11(1):32–34.
152. Bainbridge LC, Simmons HM, Elliot D. The use of automatic blood pressure monitors in the burned patient. Br J Plast Surg 1990; 43(3):322–324.
153. Talke P, Nichols RJ, Traber DL. Does measurement of systolic blood pressure with a pulse oximeter correlate with conventional methods? J Clin Monit 1990; 6:5–9.
154. Murray WB, Foster PA. The peripheral pulse wave: information overlooked. J Clin Monit 1996; 12:365–377.
155. Tavernier B, Makhotine O, Lebuffe G, et al. Systolic pressure variation as a guide to fluid therapy in patients with sepsis-induced hypotension. Anesthesiology 1998; 89:1313–1321.
156. Perel A. Assessing fluid responsiveness by the systolic pressure variation in mechanically ventilated patients. Anesthesiology 1998; 89:1309–1310.
157. Slogoff S, Keats AS, Arlund C. On the safety of radial artery cannulation. Anesthesiology 1983; 59:42–47.
158. Bedford RF. Radial arterial function following percutaneous cannulation with 18- and 20-gauge catheters. Anesthesiology 1977; 47:37–39.
159. Thomas F, Burke JP, Parker J, et al. The risk of infection related to radial versus femoral sites for arterial catheterization. Crit Care Med 1983; 11:807–812.
160. Gurman GM, Kriemerman S. Cannulation of big arteries in critically ill patients. Crit Care Med 1985; 13:217–220.
161. Purdue GF, Hunt JL. Vascular access through the femoral vessels: indications and complications. J Burn Care Rehabil 1986; 7:448–450.
162. Cilley RE. Arterial access in infants and children. Semin Pediatr Surg 1992; 3:174–180.
163. Norwood SH, Cormier B, McMahon NG, et al. Prospective study of catheter-related infection during prolonged arterial catheterization. Crit Care Med 1988; 16:836–839.
164. Frezza EE, Mezghebe H. Indications and complications of arterial catheter use in surgical or medical intensive care units: analysis of 4932 patients. Am Surg 1998; 64:127–131.
165. Kocis KC, Vermilion RP, Callow LB, et al. Complications of femoral artery cannulation for perioperative monitoring in children. J Thorac Cardiovasc Surg 1996; 112:1399–1400.
166. Graves PW, Davis AL, Maggi JC, et al. Femoral artery cannulation for monitoring in critically ill children: prospective study. Crit Care Med 1990; 18:1363–1366.
167. Randolph AG, Cook DJ, Gonzales CA, et al. Benefit of heparin in peripheral venous and arterial catheters: systematic review and meta-analysis of randomized clinical trials. Br Med J 1998; 316:969–975.
168. Sheridan RL, Weber JM, Tompkins RG. Femoral arterial catheterization in pediatric burn patients. Burns 1994; 20:451–452.
169. Franken EA, Girod D, Sequeirs FW, et al. Femoral artery spasm in children: catheter size is the principal cause. Am J Rad 1982; 138:295–298.
170. Smith-Wright DL, Green TP, Lock JE, et al. Complication of vascular catheterization in critically ill children. Crit Care Med 1984; 12:1015–1017.
171. Sellden H, Nilsson K, Eksrom-Jodal B. Radial arterial catheters in children and neonates: a prospective study. Crit Care Med 1987; 15:1106–1109.
172. Miyasaka K, Edmonds JF, Conn AW. Complication of radial artery lines in the paediatric patient. Canad Anaesth Soc J 1976; 23:9–14.
173. Soderstom CA, Wasserman DH, Dunham CM, et al. Superiority of the femoral artery for monitoring. Am J Surg 1982; 144:309–312.
174. Saint S, Matthay MA. Risk reduction in the intensive care unit. Am J Med 1998; 105:515–523.
175. Hagley MT, Marin B, Gast P, et al. Infectious and mechanical complications of central venous catheters placed by percutaneous venipuncture and over guidewire. Crit Care Med 1192; 20:1426–1430.
176. Stenzel JP, Green TP, Fuhrman BP, et al. Percutaneous femoral venous catheterizations: a prospective study of complications. J Pediatr 1989; 114:411–415.
177. Trottier SJ, Veremakis C, O'Brien J, et al. Femoral deep vein thrombosis associated with central venous catheterization: results from a prospective, randomized trial. Crit Care Med 1995; 23:52–59.
178. Venkataraman ST, Thompson AE, Orr RA. Femoral vascular catheterization in critically ill infants and children. Clin Ped 1997; 311:310–319.
179. Purdue GF, Hunt JL. Pulmonary emboli in burned patients. J Trauma 1988; 28:218–220.
180. Goldstein AM, Weber JM, Sheridan RL. Femoral venous access is safe in burned children: an analysis of 224 catheters. J Pediatr 1997; 130:442–446.
181. Kanter RK, Zimmerman JJ, Strauss RH et al. Central venous catheter insertion femoral vein: safety and effectiveness for the pediatric patient. Pediatrics 1986; 77:842–847.
182. Murr MM, Rosenquist MD, Lewis RW, et al. A prospective safety study of femoral vein versus nonfermoral vein catheterization in patients with burns. J Burn Care Rehabil 1991; 12:576–578.
183. Still JM, Law E, Thiruvaiyaru D, et al. Central line-related sepsis in acute burn patients. Am Surg 1998; 64:165–170.
184. Kealey GP, Chang P, Heinle J, et al. Prospective comparison of two management strategies of central venous catheters in burns patients. J Trauma 1995; 38:344–349.
185. Lesseva M. Central venous catheter-related bacteremia in burn patients. Scand J Infect Dis 1998; 30:585–589.
186. Eyer S, Brummitt C, Crossley K, et al. Catheter-related sepsis: prospective, randomized study of three methods of long-term catheter maintenance. Crit Care Med 1990; 18:1073–1079.
187. Sheridan RL, Weber JM, Peterson HF, et al. Central venous catheter sepsis with weekly catheter change in paediatric burn patients: an analysis of 221 catheters. Burns 1995; 21:127–129.
188. Stenzel JP, Green TP, Fuhrman BP, et al. Percutaneous central venous catherization in a pediatric intensive care unit: a survival analysis of complications. Crit Care Med 1989; 17:984–988.
189. Garrison RN, Wilson MA. Intravenous and central catheter infections. Surg Clin N Am 1994; 74:557–570.
190. American Society of Anesthesiologists. Recommendations for infection control for the practice of anesthesiology. Prevention of infection during insertion and maintenance of central venous catheters. ••: ASA, 1997.
191. Ahmed Z, Mohyuddin Z. Complications associated with different insertion techniques for Hickman catheters. Postgrad Med J 1998; 868:104–107.
192. Fraenkel D, Rickard C, Thomas P, et al. A prospective, randomized trial of rifampicin-minocycline-coated and silver-platinum-carbon-impregnated central venous catheters. Crit Care Med ••; 34(3):668–675.
193. O'Grady NP, Alexander M, Dellinger EP, et al. Guidelines for the prevention of intravascular catheter-related infections. MMWR Recomm Rep 2002; 51:1–29.
194. Chalyakunapruk N, Veenstra DdL, Lipsky BA, et al. Chlorhexidine compared with providone-iodine solution for vascular catheter-site care: a meta-analysis. Ann Intern Med 2002; 136:792–801.
195. Idris AH, Melker RJ. High-flow sheaths for pediatric fluid resuscitation: a comparison of flow rates with standard pediatric catheters. Pediatr Emerg Care 1992; 8:119–122.

196. Hodge D, Delgado-Paredes C, Fleisher G. Central and peripheral catheter flow rates in 'pediatric' dogs. Ann Emerg Med 1986; 15:1151–1154.
197. de la Roche MR, Gauthier L. Rapid transfusion of packed red blood cells: effects of dilution, pressure, and catheter size. Ann Emerg Med 1993; 22:1551–1555.
198. Millikan JA, Cain TL, Hansbrough J. Rapid volume replacement for hypovolemic shock: a comparison of techniques and equipment. J Trauma 1984; 24:428–431.
199. Dutky PA, Stevens SL, Maull KI. Factors affecting fluid resuscitation with large-bore introducer catheters. J Trauma 1989; 29:856–860.
200. Beebe DS, Beck D, Belani KG. Comparison of the flow rates of central venous catheters designed for rapid transfusion in infants and small children. Paedr Anaes 1995; 5:35–39.
201. White PF, Way WL, Trevor AJ. Ketamine — its pharmacology and therapeutic uses. Anesthesiology 1982; 56:119–136.
202. Layon AJ, Vetter TR, Hanna PG, et al. An anesthetic technique to fabricate a pressure mask for controlling scar formation from facial burns. J Burn Care Rehabil 1991; 12:349–152.
203. Maldini B. Ketamine anesthesia in children with acute burns and scalds. Acta Anaesthesiol Scand 1996; 40:1108–1111.
204. Irving GA, Butt AD. Anaesthesia for burns in children: a review of procedures practiced at Red Cross War Memorial Children's Hospital. Cape Town. Burns 1994; 20:241–243.
205. Costello TG, Cormack JR. Anaesthesia for awake craniotomy: a modern approach. J Clin Neorusci 2004; 11(1):16–19.
206. Talon MD, Woodson LC, Sherwood E. Regional sensory nerve blocks of the scalp decrease the incidence of post-operative nausea and vomiting in reconstructive burn children: A pilot study. J Burn Care Rehabil 2006; 27(2):5149.
207. Sheridan RL, Szyfelbein SK. Trends in blood conservation in burn care. Burns 2001; 27:272–276.
208. O'Mara MS, Hayetian F, Slater H, et al. Results of a protocol of transfusion threshold and surgical technique on transfusion requirements in burn patients. Burns 2005; 31:558–561.
209. Mann R, Heimbach DM, Engrav LH, et al. Changes in transfusion practices in burn patients. J Trauma 1994; 37:220–222.
210. Sittig KM, Deitch EA. Blood transfusions: for the thermally injured or for the doctor? J Trauma 1994; 36:369–372.
211. American Society of Anesthesiologists. Practice guidelines for blood component therapy: a report by the American Society of Anesthesiologists Task Force on Blood Component Therapy. Anesthesiology 1996; 84:732–747.
212. Criswell KK, Gamelli RL. Establishing transfusion needs in burn patients. Am J Surgery 2005; 189:324–326.
213. Smoot EC III. Modified use of extremity tourniquets for burn wound debridement. J Burn Care Rehabil 1996; 17:334–337.
214. Missavage AE, Bush RL, Kien ND, et al. The effect of clysed and topical epinephrine on intraoperative catecholamine levels. J Trauma 1998; 45:1074–1078.
215. Barret JP, Dziewulski P, Wolf SE, et al. Effect of topical and subcutaneous epinephrine in combination with topical thrombin in blood loss during immediate near-total burn wound excision in pediatric burned patients. Burns 1999; 25:509–513.
216. Mzezewa S, Jonsson K, Aberg M, et al. A prospective double blind randomized study comparing the need for blood transfusion with terlipressin or a placebo during early excision and grafting of burns. Burns 2004; 30:236–240.
217. Barret JP, Desai MH, Herndon DN. Massive transfusion of reconstituted whole blood is well tolerated in pediatric burn surgery. J Trauma 1999; 47:526–528.
218. Dzik WH, Kirkley SA. Citrate toxicity during massive blood transfusion. Transfus Med Rev 1988; 2:76–94.
219. Graves TA, Cioffi WG, Mason AD Jr, et al. Relationship of transfusion and infection in a burn population. J Trauma 1989; 29: 948–952.
220. Rodeberg DA, Easter AJ, Washam MA, et al. Use of a helium-oxygen mixture in the treatment of postextubation stridor in pediatric patients with burns. J Burn Care Rehabil 1995; 16(5):476–480.

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