



Introduction

Approximately 500,000 people seek medical attention annually for burn injuries in the United States. About 10% of those patients are hospitalized for their burns [1]. Although burns continue to be a major source of morbidity and mortality, improvements in care over the last 40 years have significantly reduced this burden. Many of these patients end up in the operating room for care of their burns. On arrival in the operating room, these patients have significant differences in physiology from the typical patient that should be understood by the treating anesthesiologist. Significant concerns in fluid management, airway management, and cardiovascular changes all present challenges in the initial management of burn patients in the emergency department, the intensive care unit, and in the operating room. In addition, pain management and sedation requirements may require further care by an anesthesiologist outside of the operating room. It is important to have an appreciation of the physiology of burn injury to better care for those burn patients and improve outcomes.

Burn Physiology

Burn injury is categorized by the depth of injury to the dermis and subcutaneous tissues as well as the percent of body surface area involved. Superficial burns (first degree) involve only the epidermis and do not cause significant morbidity or mortality. Partial thickness burns (second degree) involve only dermis and epidermis. Full thickness burns involve all skin layers. Full thickness burns are more likely to lead to scarring. Percent of total body surface area (TBSA) involving at least second degree burns is a strong predictor of degree of morbidity in burn patients [2]. The total body surface area involved can be calculated using the Lund Brower chart. Alternatively, the simple rule of nines can be used [3]. Severe burn injury is categorized as patients with >10% TBSA burn injury in children and >25% TBSA burn injury in adults.

Severe burn injury results in significant tissue destruction and an immediate systemic inflammatory response [4]. The initial injury breaks down the body's natural barrier to infection and alters both fluid and heat regulation. Rapid fluid losses occur due to evaporative loss from the burn surface as well as increased vascular permeability. Patients often can develop significant hypothermia both due to evaporative loss and the loss of homeostatic thermoregulators. The systemic response affects not simply the burned tissue, but tissues throughout the body. Patients can develop pulmonary and cerebral edema from increased

C. R. Herlihy, M.D. (✉) · C. Barry, M.B., B.Ch.
University of Cincinnati Medical Center,
Cincinnati, OH, USA
e-mail: herlihr@ucmail.uc.edu;
barryca@ucmail.uc.edu

permeability, acute respiratory distress syndrome (ARDS), and renal failure from fluid shifts and severe hypovolemia. The systemic response to a burn injury can be predicted in two phases. The initial phase of burn shock (ebb phase) begins immediately and lasts for approximately the first 48 h. After this, a hypermetabolic (flow) phase begins that can last months after the burn injury (Table 78.1) [3]. An understanding of these changes is key to management of these patients throughout their injury course.

Burn Shock Physiology

Significant burn injury causes a release of inflammatory mediators at the site of the injury. These mediators lead to significant capillary leak. In a small burn this leads to localized edema at the burn site. With larger burns this cascade of inflammation creates systemic capillary leak leading to loss of intravascular fluid and burn

shock [5]. The flow of plasma out of the vascular space leads directly to hemoconcentration and requires significant fluid resuscitation to maintain circulating volume. The large volume fluid resuscitation continues to leak into the extravascular space and cause complications associated with edema including respiratory failure and compartment syndrome. Despite adequate resuscitation, patients initially have an elevation in their hematocrit. Without concomitant trauma, these patients rarely require blood product transfusion in their initial presentation.

Many formulae exist to calculate the appropriate volume for fluid resuscitation for burns; the most famous is the Parkland Formula ($4 \text{ mL} \times \text{Ideal body weight} \times \% \text{TBSA}$ with $\frac{1}{2}$ given over the first 8 h and the remainder given over the following 16 h) [6]. The Parkland formula tends to overload patients with fluid, leading to increased incidence of compartment syndrome and edema. Other rules have been suggested including the rule of ten's

Table 78.1 Effect of burns on different organ systems, both resulting from shock and increased metabolism

	Burn shock	Hypermetabolism
Cardiovascular	Hypovolemia	Increased cardiac output
	Decreased cardiac output	Increased resting heart rate
	Increased systemic vascular resistance (SVR)	Hypertension
	Decreased venous oxygen saturation (SvO ₂)	Decreased SVR
		Increased SvO ₂
	Altered myocardial contractility	
Respiratory	Pulmonary edema	ARDS
	Airway edema	Pneumonia
	Inhalation injury	Tracheal stenosis
		Inhalation injury
Hematologic	Hemoconcentration	Anemia
	Thrombocytopenia	Thrombocytosis
		Coagulopathy
Renal	Decreased glomerular filtration rate (GFR)	Increased GFR
	Oliguria	Tubular dysfunction
	Myoglobinuria	
Hepatic	Decreased perfusion	Increased perfusion
		Increased drug clearance
Neurologic	Increased intracranial pressure	Delirium
	Cerebral Edema	PTSD
Other	Generalized edema	Increased core body temperature
	Compartment syndrome	Muscle catabolism
		Increased metabolic rate
		Insulin resistance

(10 mL/h \times %TBSA = hourly rate) [7] or the modified Brooke formula (2 mL \times ideal body weight \times %TBSA with $\frac{1}{2}$ given over the first 8 h and the remainder over the following 16 h) [8]. These calculations should be used only to determine an initial rate for fluid resuscitation, more fluid does not necessarily decrease mortality. Resuscitation should then be titrated to physiological endpoints, most commonly urine output. The rate should be adjusted hourly based on the patient's urine output. Algorithms for resuscitation often aim for a goal urine output of 0.3–1 mL/kg per hour [9]. Impaired renal function may prove difficult for titration of fluid resuscitation. Other markers of resuscitation can be used for a more complete picture. In large burns, an arterial line may be placed for close monitoring of hemodynamics. This also allows the use of pulse contour analysis. Stroke volume variation as well as central venous pressure can be followed as a trend to evaluate adequacy of volume resuscitation. Cardiac evaluation can be easily performed with bedside ultrasonography. If evaluation of resuscitation is complicated or confusing, a pulmonary artery catheter may be helpful. In burn patients, it is important to avoid fluid boluses; rather, adjust hourly fluid rate to achieve adequate circulating volume without fluid overload. Initial resuscitation should be done with crystalloid solutions; usually Lactated Ringers or Plasmalyte solution is recommended. Albumin infusion may reduce mortality and incidence of compartment syndrome if patients are exceeding their predicted fluid resuscitation volume [10].

Inadequate volume resuscitation will cause hypovolemic shock and multi-organ dysfunction. Some lab markers that may be useful to trend include lactate and base deficit. Complete blood counts should also be followed monitoring for both anemia and hemoconcentration. Arterial blood gases will be helpful as patients with hypermetabolism may require higher than expected minute ventilation. Over resuscitation can increase morbidity and mortality. Risks are related to volume overload and increased vascular permeability. Complications of over resuscitation include pulmonary edema, respiratory

failure, pericardial and pleural effusions, abdominal and limb compartment syndromes, and ileus [6, 11, 12]. Vasopressors may be required to avoid over resuscitation and complications from volume overload. Patients may require escharotomies to prevent compartment syndrome. If there is a concern for abdominal compartment syndrome, bladder pressures should be monitored during the resuscitation phase.

Additionally, in the first 24–48 h, burned patients experience a significant decrease in cardiac output with decreased cardiac contractility. This occurs despite adequate volume resuscitation and is due to direct myocardial depression [13]. Increased pulmonary and systemic vascular resistance contribute to decreased perfusion throughout the body. All of these changes can lead to metabolic acidosis and mixed venous desaturation. Significant fluid shifts in this context lead to renal dysfunction and possibly renal failure. Renal dysfunction can further complicate treatment and possibly lead to over resuscitation, as fluid resuscitation is most often titrated to maintain a goal urine output.

Hypermetabolism Physiology

After about 48 h, the hypermetabolic phase of the burn injury begins. This flow phase lasts throughout the healing process and can last for months to years after the burn. The cardiac output transitions from low to high with increased stroke volumes [14]. Patients remain tachycardic and later can develop cardiac dysfunction due to this hyperactivity [13]. Systemic vascular resistance decreases and these changes can lead to blood loss. Lungs can be damaged due to continued pulmonary edema or ARDS even in the absence of inhalation injury. Kidneys exhibit increased GFR but decreased tubular function [15]. Hepatic metabolic function can alter drug clearance. Coagulation factor metabolism decreases. Hematopoiesis decreases resulting in long lasting anemia. Patients also become immunologically compromised due to poor WBC production.

This phase is also associated with a significant increase in metabolism throughout the body.

Protein breakdown and muscle wasting is a key component of this stage and adequate nutrition is important to minimize long term consequences and enhance healing. Nutrition should be initiated as soon as the patient is stabilized and the initial resuscitation period is over. Glucose and fat metabolism is also altered. Hyperglycemia is common and insulin is often required [16, 17]. Untreated hyperglycemia can contribute to increased infections and mortality.

Several agents have been studied as treatment of hypermetabolism with mixed results. Oxandralone is an anabolic agent that has been studied, and in one RCT this agent has shown to maintain lean body mass and improve hepatic protein synthesis [14]. Propranolol, a beta blocker, has also been studied and has been shown to reduce energy expenditure and accelerate wound healing [18, 19]. There is no consensus on which agents should be used for hypermetabolism treatment, and it is unknown if they reduce morbidity or mortality.

CO₂ production increases in this phase of injury and can create acidosis. Conventional ventilation may still result in a respiratory acidosis or an uncorrected metabolic acidosis. At the same time, the patients begin to show signs of inhalation injury, pulmonary edema, and ARDS. Lung protective ventilation with tidal volumes of 6–8 mL/kg should be used to prevent further lung injury and manage ARDS [20]. Occasionally, this is not sufficient to treat this acidosis and some patients may require tidal volumes >8–10 mL/kg IBW to control their acidosis [21]. Alternatively, if patients are having trouble with oxygenation or ventilation, high frequency percussive ventilation can be used to ventilate patients [22].

Table 78.1 highlights effect of burns on different organ systems, both resulting from shock and increased metabolism.

Inhalation Injury

Inhalation injury is a term used to describe both direct injury to the airway caused by hot gases, steam and chemical injury to the airways and alveoli due to inhaled toxins. This can occur in up

to 35% of burn victims. Isolated inhalation injury carries about 10% mortality; however, it will significantly increase mortality from burn injury [23, 24]. Patients with inhalation injury require higher volume fluid resuscitation than anticipated for their %TBSA burn. Airway obstruction is the initial concern in patients who present with possible inhalation injury. Direct burns to the larynx can result in significant injury and poor outcomes if overlooked [25]. Swelling may not occur initially, but can develop during resuscitation. In these patients it is important to secure the airway early because edema can progress rapidly leading to a compromised airway that may be difficult to intubate.

Direct thermal injury to the distal airways can be devastating but occurs rarely unless steam is inhaled. Instead, distal airways are injured by chemical injury from smoke and combustion. The mucociliary clearance is damaged, resulting in decreased clearance from the airways. Oxygenation is impaired due to inactivated surfactant and collapse of alveoli [26]. Inhalation injury is initially suspected in a fire in an enclosed area, and a high level of clinical suspicion is important in those circumstances. Other signs and symptoms include facial burns, singed nasal hairs, stridor, and carbonaceous sputum. Evaluation of the airways with bronchoscopy is the primary method for diagnosing inhalation injury [27, 28]. Treatment for inhalation injury includes N acetyl cysteine, inhaled heparin, bronchodilators, and good pulmonary toilet in addition to supportive therapy [28, 29].

Often patients who are diagnosed with inhalation injury also have exposure to other substances. Carbon monoxide is commonly seen in patients with suspected inhalation injury. A co-oximeter is used to diagnose carbon monoxide poisoning. Carbon monoxide has increased affinity for hemoglobin compared to oxygen. The presence of carbon monoxide shifts the oxyhemoglobin dissociation curve to the left, impairing oxygen delivery to the tissues. Administration of 100% oxygen decreases the half-life of carboxyhemoglobin [30, 31]. Cyanide is another poisonous gas that can produce profound acidosis and unstable hemodynamics along with an altered

mental status. Treatment with sodium thiosulfate or hydroxocobalamin is important with suspicion of cyanide poisoning [32, 33].

Patients are at risk for pulmonary edema throughout their hospital course. ARDS and acute lung injury are both concerns given the high volume fluid resuscitation needed and blood transfusions that these patients often require [34]. This contributes to increased mortality in patients, even if they do not present with an inhalation injury.

Infection

Infections are a major cause of death in burned patients [35]. A major skin function is to provide a barrier to microorganisms, and this is damaged in burn injuries. Mucociliary clearance will be decreased in inhalation injury. Patients are often febrile due to hypermetabolism, but infection should be aggressively searched for and treated. After the initial resuscitation phase, any unnecessary urinary catheters or vascular access devices should be removed. Early burn excision reduces the risk of wound infection.

Pain Management in Burn Patients

Burn patients experience significant pain from the moment they are injured. Acutely, burn patients require multiple painful procedures to care for their wounds. Additionally, dressing changes both before and after excision can be incredibly painful to patients. Adequate pain control is also an essential part of the patient's ability to participate in successful rehabilitation [36]. Additionally, patients quickly develop tolerance to medications due to their hypermetabolic state. This needs to be consistently addressed throughout their injury course.

Pain in burn patients is a significant issue in the acute phase of injury and can continue to persist through a patient's rehabilitation and for years post injury [37]. Inadequate pain control has been shown to increase the risk of depression and PTSD in burn patients [38, 39]. Achieving

adequate pain control in patients is therefore very important to their long term recovery.

Opioids are the cornerstone of management of acute burn pain. Patients with major burns require both background pain control along with intermittent procedural pain control to address pain associated with OR procedures and dressing changes [40]. Most often these patients are placed on continuous opioid therapy that can be titrated; typically, this is achieved through continuous IV infusions or patient-controlled analgesia (PCA) [41]. This allows for adjustments as patients pharmacodynamics change. Opioids should be titrated to effect in burn patients, and opioid requirements are often increased compared to non-burned patients. Methadone is often used as a long acting opioid with NMDA receptor activity to treat background pain [42].

Non opioid analgesia is an important supplement to opioid analgesia. Ketamine is often used in the management of pain in burn patients [43]. It is used as a sedative in procedures, or it can be used in patients with refractory pain as an infusion. Conscious sedation with bolus doses of ketamine can be useful during long and painful dressing changes. Dexmedetomidine is another adjunct that can be very useful in pain management in refractory patients [44, 45]. Maintaining anxiolysis in these patients is important to avoid escalation of pain [46]. Other useful adjuncts include acetaminophen and non-steroidal anti-inflammatory (NSAID) use [39, 47]. These medications help to minimize the requirement for opioid therapy and can be used as sole agents in patients with smaller burns.

In patients who present with large burns, neuropathic pain should be considered due to the direct nerve injury sustained. Alleviating this pain can be very important for long term improvement in pain status. Gabapentin and pregabalin are the primary options for treatment. Antidepressant medications can also be considered for this treatment [40].

Local anesthetics are often used with success in burn patients. Tumescence local anesthetics with or without epinephrine can be injected into donor sites to reduce pain from skin harvesting procedures. Regional anesthesia is an option for

many of these patients. This can be used both for the acute burn and for donor site pain. Options for regional anesthesia include peripheral blocks, catheters, and neuraxial blocks [48]. One limitation of this technique is infection risk, so avoiding burned skin for placement of catheters is important. The thigh is often used as a donor site for skin grafts, therefore lateral femoral cutaneous and fascia iliaca nerve blocks are often used for pain at this site [49].

Practical Management of Burn Patients

Burn patients often require multiple trips to the operating room for escharotomies, burn excision and grafting, reconstructive surgery, and tracheostomies. Prior to bringing a patient with a large burn into the operating room, it is important to begin by preparing the room. Due to the loss of temperature regulation by the skin, these patients can lose heat very quickly. It is the standard to prepare a warm room to minimize heat loss although this can be controversial [50]. It is also important to note the patient's preoperative temperature, as hypermetabolic patients can be hyperthermic at baseline. Decreased body temperature can lead to increased oxygen consumption, increased blood loss, and increased risk of infection [34]. Blood and fluid warmers are important to maintain temperature. Additionally, warming blankets with fluid or blown air can be helpful to maintain temperature. Special care is required in patient positioning in the operating room to avoid damage to the skin or grafts.

Early excision of burn injury and grafting to cover the wound is important to minimize both morbidity and mortality [51, 52]. Often burn patients are in the operating room soon after their injuries, occasionally even while they are still undergoing resuscitation. Because of this, burn patients are often hemodynamically unstable when they are first taken to the operating room and require consistent active management. Burn patients may also have additional traumatic injuries related to the burn event that may require special management. Outside of the operating room

burn patients often require sedation for painful procedures [43]. These procedures are often done with sedation managed by the anesthesia team.

Airway Management

Airway management in these patients can be complicated due to swelling. It is important to have a good airway exam early to prepare for any difficulties. Limited mouth opening due to burns or scarring can complicate airway management. Laryngeal burns are a concern, and if possible, a good look at the larynx is important on intubation for early intervention. Bronchoscopic evaluation for inhalation injury in patients where it is suspected can be beneficial. Patients need to be evaluated also for possible difficult mask ventilation due to facial dressings or wounds [3]. Additionally, securing the airway can be difficult as tape often does not adhere well to burn injuries. Ties can be a concern due to swelling. Securing the airway to the teeth with wire or suture is an option. Stapling tape to the skin is an alternate method to secure the airway. As patients progress through their hospital stay, neck contractures can make airway management increasingly difficult. Laryngeal mask airways (LMA) have been shown to be both safe and effective airway management tools to assist in difficult airways after burns [53]. Fiber optic intubation is occasionally a required technique if the airway appears difficult [3]. If a patient needs to be intubated, consideration for pulmonary toilet and frequent bronchoscopies should be given in choosing an endotracheal tube. Intra-operative ventilation may be difficult due to associated pulmonary edema or ARDS. If the patient has circumferential chest wall burns, this may cause restrictive physiology.

Fluid Management

Fluid management in the operating room is especially important in burned patients. Patients who are still in their initial resuscitation must continue the resuscitation throughout surgery. Large fluid boluses put patients at risk for fluid overload and

compartment syndromes, therefore, it is important to consistently adjust their maintenance rate [12]. Monitoring urine output and vital signs and adjusting fluid rates accordingly is especially important (Goal rate of hourly urine output 0.3–1 mL/kg). In the operating room, this becomes more of a challenge due to insensible fluid losses and blood loss; therefore, consistent vigilance is required.

Excision of burn wounds can cause significant blood loss, which can be incredibly difficult to monitor. The hyperdynamic state of the patient can contribute to increased blood loss. Blood loss during excision has been reported to be 2.6–3.4% of blood volume for every 1%TBSA excised [54]. This can occur very rapidly. Estimating blood loss is difficult as much of the loss cannot be suctioned and sponges contain both blood and irrigation fluid. Significant amounts of blood loss can also collect beneath the patient or in dressings [55]. It is important to be vigilant in monitoring for blood loss. Many techniques have been studied to minimize blood loss in these procedures. Topical thrombin, brisk operative pace, use of tourniquets, injection or topical application of vasoconstrictors have all been attempted [56, 57]. No one method has been shown superior [58]. Often, staged procedures are necessary to avoid hemorrhagic shock in these patients.

Given this predictable blood loss, it is important to be prepared. A type and screen should be performed preoperatively and blood should be available when large blood loss is anticipated. Blood loss should be aggressively treated as it is easy to “get behind” once excision has started. When the patient’s predicted blood loss will likely decrease the hematocrit below the patient’s transfusion threshold, it can be useful to start blood preoperatively given how rapidly patients can bleed. It is important to avoid over transfusion, as transfusion can be associated with increased risk of infections and mortality [59].

Tumescent crystalloid with a vasoconstrictor can be injected by the surgeon into the subcutaneous tissue to minimize blood loss while excising burned tissue. Occasionally, local anesthetic may be added to the tumescent crystalloid to assist with pain control post-operatively. Significant amounts of this fluid can be injected into tissue, often

exceeding 100 mL/kg. This fluid is then gradually absorbed into the vasculature over the following 24–48 h. This can create a delayed fluid overload which must be monitored, especially if patients are returning for subsequent procedures or requiring additional fluid replacement.

Pharmacologic Management

Succinylcholine use is a concern in burned patients. It is generally safe to use within 48 h of burn injury. After 48 h, an up regulation of extra-junctional acetylcholine receptors put patients at risk for an exaggerated hyperkalemic response after administration of succinylcholine [60]. The severe hyperkalemia can lead to cardiac arrest. Other anesthetic medications are considered safe. There is a decreased sensitivity to non-depolarizing muscle relaxants noted in burned patients [61]. Increased volume of distribution as well as altered plasma proteins may lead to unpredictable drug pharmacokinetics [62]. Drug metabolism may be altered due to hypermetabolism as well as renal or hepatic dysfunction.

Vascular Access

Intravenous access may be difficult in extensive burn injuries. If possible, vascular access should be obtained from areas of unburned skin to minimize risk of infection. These patients should have at least two large bore IV lines for fluid resuscitation and blood administration. They often require central lines for long term access and vasopressor administration. Securing IVs to burned skin may be difficult as adhesive dressings will not stay in place. A stitch may be used to secure IVs. Central lines should be monitored closely and meticulous care is required to avoid line infections.

Monitoring

Patients with large burn injury present multiple challenges when it comes to monitoring. Transmission pulse oximetry does not work well

through severely burned skin; therefore, alternate unburned sites may need to be considered [63, 64]. Based on the extent of burn injury, EKG electrodes may not stick to the patient. Needle electrodes or an esophageal catheter with an EKG electrode can be useful to obtain EKG monitoring [65]. Core temperature monitoring is essential to maintain body temperature during surgery. Monitoring invasive blood pressure is useful to obtain accurate blood pressure readings depending on the surgical sites. CVP monitoring can be helpful in patients with ongoing resuscitation.

Nutrition

As detailed above, the hypermetabolic response after burn injury requires significant nutritional support. Burn injured patients may undergo multiple surgical procedures to excise eschar and cover their wounds. Periods of fasting have been shown to cause significant nutritional deficits in these patients, which can lead to poor wound healing and malnutrition [66]. Studies have shown safety in post pyloric feeding through surgery [67]. Parenteral nutrition is occasionally used when enteral feeding is not an option, however, this presents the risk of infection and increased mortality [68, 69].

Burn Reconstruction

After initial burns are healed, scarring can be a recurrent problem. Many patients will require surgical treatment of their burn scars. Patients with significant burn history often present with very difficult IV access due to scarring and contractures [70]. It can be very useful to have an ultrasound available for IV access. In addition, airway management can be complicated by burn scar contractures to the neck or mouth. Fiber optic intubation or LMA placement can be beneficial in patients with a suspected difficult intubation. Patients with significant previous injuries often still have resistance to non-depolarizing muscle relaxants. They also have higher tolerance with opiate drugs and should be dosed accordingly.

Reference

1. American Burn Association. Sources: National Hospital Ambulatory Medical Care Survey: 2011 Emergency Department Summary Tables (accessed on January 22, 2015, at http://www.cdc.gov/nchs/ahcd/web_tables.htm#2011). Fire/Smoke Inhalation Deaths:3,275 This total includes 2,745 deaths from residential fires, 310 from vehicle crash fires, and 220 from other sources. One civilian fire death occurs every 2 hours and 41 minutes. The odds of a U.S. resident dying from exposure to fire, flames or smoke is 1 in 1442. Fire and inhalation deaths are combined because deaths from thermal burns in fires cannot always be distinguished from deaths from inhalation of toxins in smoke. 2017. http://www.ameriburn.org/resources_factsheet.php.
2. Tobiasen J, Hiebert JH, Edlich RF. Prediction of burn mortality. *Surg Gynecol Obstet.* 1982;154(5):711–4.
3. Bittner EA, Shank E, Woodson L, Martyn JA. Acute and perioperative care of the burn-injured patient. *Anesthesiology.* 2015;122(2):448–64. <https://doi.org/10.1097/ALN.0000000000000559>.
4. Finnerty CC, Herndon DN, Przkora R, Pereira CT, Oliveira HM, Queiroz DM, et al. Cytokine expression profile over time in severely burned pediatric patients. *Shock.* 2006;26(1):13–9. <https://doi.org/10.1097/01.shk.0000223120.26394.7d>.
5. Arturson G, Jonsson CE. Transcapillary transport after thermal injury. *Scand J Plast Reconstr Surg.* 1979;13(1):29–38.
6. Alvarado R, Chung KK, Cancio LC, Wolf SE. Burn resuscitation. *Burns.* 2009;35(1):4–14. <https://doi.org/10.1016/j.burns.2008.03.008>.
7. Chung KK, Salinas J, Renz EM, Alvarado RA, King BT, Barillo DJ, et al. Simple derivation of the initial fluid rate for the resuscitation of severely burned adult combat casualties: in silico validation of the rule of 10. *J Trauma.* 2010;69(Suppl 1):S49–54. <https://doi.org/10.1097/TA.0b013e3181e425f1>.
8. Chung KK, Wolf SE, Cancio LC, Alvarado R, Jones JA, McCorcle J, et al. Resuscitation of severely burned military casualties: fluid begets more fluid. *J Trauma.* 2009;67(2):231–7. <https://doi.org/10.1097/TA.0b013e3181ac68cf>; discussion 7.
9. Pham TN, Cancio LC, Gibran NS, American Burn Association. American burn association practice guidelines burn shock resuscitation. *J Burn Care Res.* 2008;29(1):257–66. <https://doi.org/10.1097/BCR.0b013e31815f3876>.
10. Navickis RJ, Greenhalgh DG, Wilkes MM. Albumin in burn shock resuscitation: a meta-analysis of controlled clinical studies. *J Burn Care Res.* 2016;37(3):e268–78. <https://doi.org/10.1097/BCR.0000000000000201>.
11. Klein MB, Hayden D, Elson C, Nathens AB, Gamelli RL, Gibran NS, et al. The association between fluid administration and outcome following major burn: a multicenter study. *Ann Surg.* 2007;245(4):622–8. <https://doi.org/10.1097/01.sla.0000252572.50684.49>.

12. Oda J, Yamashita K, Inoue T, Harunari N, Ode Y, Mega K, et al. Resuscitation fluid volume and abdominal compartment syndrome in patients with major burns. *Burns*. 2006;32(2):151–4. <https://doi.org/10.1016/j.burns.2005.08.011>.
13. Carleton SC. Cardiac problems associated with burns. *Cardiol Clin*. 1995;13(2):257–62.
14. Jeschke MG, Finnerty CC, Suman OE, Kulp G, Mlcak RP, Herndon DN. The effect of oxandrolone on the endocrinologic, inflammatory, and hypermetabolic responses during the acute phase postburn. *Ann Surg*. 2007;246(3):351–60. <https://doi.org/10.1097/SLA.0b013e318146980e>; discussion 60–2.
15. Chrysopoulou MT, Jeschke MG, Dziejewski P, Barrow RE, Herndon DN. Acute renal dysfunction in severely burned adults. *J Trauma*. 1999;46(1):141–4.
16. Gore DC, Chinkes D, Hegggers J, Herndon DN, Wolf SE, Desai M. Association of hyperglycemia with increased mortality after severe burn injury. *J Trauma*. 2001;51(3):540–4.
17. Ray JJ, Meizoso JP, Allen CJ, Teisch LF, Yang EY, Foong HY, et al. Admission hyperglycemia predicts infectious complications after burns. *J Burn Care Res*. 2017;38(2):85–9. <https://doi.org/10.1097/BCR.0000000000000381>.
18. Ali A, Herndon DN, Mamachen A, Hasan S, Andersen CR, Grogans RJ, et al. Propranolol attenuates hemorrhage and accelerates wound healing in severely burned adults. *Crit Care*. 2015;19:217. <https://doi.org/10.1186/s13054-015-0913-x>.
19. Herndon DN, Rodriguez NA, Diaz EC, Hegde S, Jennings K, Mlcak RP, et al. Long-term propranolol use in severely burned pediatric patients: a randomized controlled study. *Ann Surg*. 2012;256(3):402–11. <https://doi.org/10.1097/SLA.0b013e318265427e>.
20. Peck MD, Koppelman T. Low-tidal-volume ventilation as a strategy to reduce ventilator-associated injury in ALI and ARDS. *J Burn Care Res*. 2009;30(1):172–5. <https://doi.org/10.1097/BCR.0b013e3181923c32>.
21. Sousse LE, Herndon DN, Andersen CR, Ali A, Benjamin NC, Granchi T, et al. High tidal volume decreases adult respiratory distress syndrome, atelectasis, and ventilator days compared with low tidal volume in pediatric burned patients with inhalation injury. *J Am Coll Surg*. 2015;220(4):570–8. <https://doi.org/10.1016/j.jamcollsurg.2014.12.028>.
22. Chung KK, Wolf SE, Renz EM, Allan PF, Aden JK, Merrill GA, et al. High-frequency percussive ventilation and low tidal volume ventilation in burns: a randomized controlled trial. *Crit Care Med*. 2010;38(10):1970–7. <https://doi.org/10.1097/CCM.0b013e3181eb9d0b>.
23. El-Helbawy RH, Ghareeb FM. Inhalation injury as a prognostic factor for mortality in burn patients. *Ann Burns Fire Disasters*. 2011;24(2):82–8.
24. Kadri SS, Miller AC, Hohmann S, Bonne S, Nielsen C, Wells C, et al. Risk factors for in-hospital mortality in smoke inhalation-associated acute lung injury: data from 68 United States Hospitals. *Chest*. 2016;150(6):1260–8. <https://doi.org/10.1016/j.chest.2016.06.008>.
25. Valdez TA, Desai U, Ruhl CM, Nigri PT. Early laryngeal inhalation injury and its correlation with late sequelae. *Laryngoscope*. 2006;116(2):283–7. <https://doi.org/10.1097/01.mlg.0000197932.09386.0e>.
26. Nieman GF, Clark WR, Wax SD, Webb SR. The effect of smoke inhalation on pulmonary surfactant. *Ann Surg*. 1980;191(2):171–81.
27. Miller K, Chang A. Acute inhalation injury. *Emerg Med Clin North Am*. 2003;21(2):533–57.
28. Walker PF, Buehner MF, Wood LA, Boyer NL, Driscoll IR, Lundy JB, et al. Diagnosis and management of inhalation injury: an updated review. *Crit Care*. 2015;19:351. <https://doi.org/10.1186/s13054-015-1077-4>.
29. Miller AC, Elamin EM, Suffredini AF. Inhaled anti-coagulation regimens for the treatment of smoke inhalation-associated acute lung injury: a systematic review. *Crit Care Med*. 2014;42(2):413–9. <https://doi.org/10.1097/CCM.0b013e3182a645e5>.
30. Kao LW, Nañagas KA. Carbon monoxide poisoning. *Med Clin North Am*. 2005;89(6):1161–94. <https://doi.org/10.1016/j.mcna.2005.06.007>.
31. Varon J, Marik PE, Fromm RE, Gueler A. Carbon monoxide poisoning: a review for clinicians. *J Emerg Med*. 1999;17(1):87–93.
32. Baud FJ, Barriot P, Toffis V, Riou B, Vicaut E, Lecarpentier Y, et al. Elevated blood cyanide concentrations in victims of smoke inhalation. *N Engl J Med*. 1991;325(25):1761–6. <https://doi.org/10.1056/NEJM199112193252502>.
33. Geller RJ, Barthold C, Saiers JA, Hall AH. Pediatric cyanide poisoning: causes, manifestations, management, and unmet needs. *Pediatrics*. 2006;118(5):2146–58. <https://doi.org/10.1542/peds.2006-1251>.
34. Oda J, Kasai K, Noborio M, Ueyama M, Yukioka T. Hypothermia during burn surgery and postoperative acute lung injury in extensively burned patients. *J Trauma*. 2009;66(6):1525–9. <https://doi.org/10.1097/TA.0b013e3181a51f35>; discussion 9–30.
35. Church D, Elsayed S, Reid O, Winston B, Lindsay R. Burn wound infections. *Clin Microbiol Rev*. 2006;19(2):403–34. <https://doi.org/10.1128/CMR.19.2.403-434.2006>.
36. Faucher L, Furukawa K. Practice guidelines for the management of pain. *J Burn Care Res*. 2006;27(5):659–68. <https://doi.org/10.1097/01.BCR.0000238117.41490.00>.
37. Duffy JR, Warburg FE, Koelle SF, Werner MU, Nielsen PR. Pain-related psychological distress, self-rated health and significance of neuropathic pain in Danish soldiers injured in Afghanistan. *Acta Anaesthesiol Scand*. 2015;59(10):1367–76. <https://doi.org/10.1111/aas.12579>.
38. Sheridan RL, Stoddard FJ, Kazis LE, Lee A, Li NC, Kagan RJ, et al. Long-term posttraumatic stress symptoms vary inversely with early opiate dosing in children recovering from serious burns: effects durable at

- 4 years. *J Trauma Acute Care Surg.* 2014;76(3):828–32. <https://doi.org/10.1097/TA.0b013e3182ab111c>.
39. Pardesi O, Fuzaylov G. Pain management in pediatric burn patients: review of recent literature and future directions. *J Burn Care Res.* 2016;38(6):335–47. <https://doi.org/10.1097/BCR.0000000000000470>.
 40. Retrouvey H, Shahrokhi S. Pain and the thermally injured patient—a review of current therapies. *J Burn Care Res.* 2015;36(2):315–23. <https://doi.org/10.1097/BCR.0000000000000073>.
 41. Rovers J, Knighton J, Neligan P, Peters W. Patient-controlled analgesia in burn patients: a critical review of the literature and case report. *Hosp Pharm.* 1994;29(2):106, 8–11.
 42. Williams PI, Sarginson RE, Ratcliffe JM. Use of methadone in the morphine-tolerant burned paediatric patient. *Br J Anaesth.* 1998;80(1):92–5.
 43. Owens VF, Palmieri TL, Comroe CM, Conroy JM, Scavone JA, Greenhalgh DG. Ketamine: a safe and effective agent for painful procedures in the pediatric burn patient. *J Burn Care Res.* 2006;27(2):211–6. <https://doi.org/10.1097/01.BCR.0000204310.67594.A1>; discussion 7.
 44. Walker J, Maccallum M, Fischer C, Kopcha R, Saylor R, McCall J. Sedation using dexmedetomidine in pediatric burn patients. *J Burn Care Res.* 2006;27(2):206–10. <https://doi.org/10.1097/01.BCR.0000200910.76019.CF>.
 45. Sheridan R, Stoddard F, Querzoli E. Management of background pain and anxiety in critically burned children requiring protracted mechanical ventilation. *J Burn Care Rehabil.* 2001;22(2):150–3.
 46. Ratcliff SL, Brown A, Rosenberg L, Rosenberg M, Robert RS, Cuervo LJ, et al. The effectiveness of a pain and anxiety protocol to treat the acute pediatric burn patient. *Burns.* 2006;32(5):554–62. <https://doi.org/10.1016/j.burns.2005.12.006>.
 47. Meyer WJ, Nichols RJ, Cortiella J, Villarreal C, Marvin JA, Blakeney PE, et al. Acetaminophen in the management of background pain in children post-burn. *J Pain Symptom Manag.* 1997;13(1):50–5.
 48. Dadure C, Acosta C, Capdevila X. Perioperative pain management of a complex orthopedic surgical procedure with double continuous nerve blocks in a burned child. *Anesth Analg.* 2004;98(6):1653–5, table of contents.
 49. Cuiagnet O, Pirson J, Boughrough J, Duville D. The efficacy of continuous fascia iliaca compartment block for pain management in burn patients undergoing skin grafting procedures. *Anesth Analg.* 2004;98(4):1077–81, table of contents.
 50. Rizzo JA, Rowan MP, Driscoll IR, Chan RK, Chung KK. Perioperative temperature management during burn care. *J Burn Care Res.* 2017;38(1):e277–e83. <https://doi.org/10.1097/BCR.0000000000000371>.
 51. Ong YS, Samuel M, Song C. Meta-analysis of early excision of burns. *Burns.* 2006;32(2):145–50. <https://doi.org/10.1016/j.burns.2005.09.005>.
 52. Tompkins RG, Remensnyder JP, Burke JF, Tompkins DM, Hilton JF, Schoenfeld DA, et al. Significant reductions in mortality for children with burn injuries through the use of prompt eschar excision. *Ann Surg.* 1988;208(5):577–85.
 53. McCall JE, Fischer CG, Schomaker E, Young JM. Laryngeal mask airway use in children with acute burns: intraoperative airway management. *Paediatr Anaesth.* 1999;9(6):515–20.
 54. Budny PG, Regan PJ, Roberts AH. The estimation of blood loss during burns surgery. *Burns.* 1993;19(2):134–7.
 55. Housinger TA, Lang D, Warden GD. A prospective study of blood loss with excisional therapy in pediatric burn patients. *J Trauma.* 1993;34(2):262–3.
 56. Beausang E, Orr D, Shah M, Dunn KW, Davenport PJ. Subcutaneous adrenaline infiltration in paediatric burn surgery. *Br J Plast Surg.* 1999;52(6):480–1. <https://doi.org/10.1054/bjps.1999.3161>.
 57. Mitchell RT, Funk D, Spiwak R, Logsetty S. Phenylephrine tumescence in split-thickness skin graft donor sites in surgery for burn injury—a concentration finding study. *J Burn Care Res.* 2011;32(1):129–34. <https://doi.org/10.1097/BCR.0b013e318204b39b>.
 58. Sterling JP, Heimbach DM. Hemostasis in burn surgery—a review. *Burns.* 2011;37(4):559–65. <https://doi.org/10.1016/j.burns.2010.06.010>.
 59. Palmieri TL, Caruso DM, Foster KN, Cairns BA, Peck MD, Gamelli RL, et al. Effect of blood transfusion on outcome after major burn injury: a multicenter study. *Crit Care Med.* 2006;34(6):1602–7. <https://doi.org/10.1097/01.CCM.0000217472.97524.0E>.
 60. Martyn JA, Richtsfeld M. Succinylcholine-induced hyperkalemia in acquired pathologic states: etiologic factors and molecular mechanisms. *Anesthesiology.* 2006;104(1):158–69.
 61. Jaehde U, Sörgel F. Clinical pharmacokinetics in patients with burns. *Clin Pharmacokinet.* 1995;29(1):15–28. <https://doi.org/10.2165/00003088-199529010-00003>.
 62. Blanchet B, Jullien V, Vinsonneau C, Tod M. Influence of burns on pharmacokinetics and pharmacodynamics of drugs used in the care of burn patients. *Clin Pharmacokinet.* 2008;47(10):635–54. <https://doi.org/10.2165/00003088-200847100-00002>.
 63. Coté CJ, Daniels AL, Connolly M, Szyfelbein SK, Wickens CD. Tongue oximetry in children with extensive thermal injury: comparison with peripheral oximetry. *Can J Anaesth.* 1992;39(5 Pt 1):454–7. <https://doi.org/10.1007/BF03008709>.
 64. Pal SK, Kyriacou PA, Kumaran S, Fadheel S, Emamdee R, Langford RM, et al. Evaluation of oesophageal reflectance pulse oximetry in major burns patients. *Burns.* 2005;31(3):337–41. <https://doi.org/10.1016/j.burns.2004.10.025>.
 65. Reid M, Shaw P, Taylor RH. Oesophageal ECG in a child for burns surgery. *Paediatr Anaesth.* 1997;7(1):73–6.
 66. Pearson KS, From RP, Symreng T, Kealey GP. Continuous enteral feeding and short fasting periods enhance perioperative nutrition in patients with burns. *J Burn Care Rehabil.* 1992;13(4):477–81.

67. Jenkins ME, Gottschlich MM, Warden GD. Enteral feeding during operative procedures in thermal injuries. *J Burn Care Rehabil.* 1994;15(2):199–205.
68. Chen Z, Wang S, Yu B, Li A. A comparison study between early enteral nutrition and parenteral nutrition in severe burn patients. *Burns.* 2007;33(6):708–12. <https://doi.org/10.1016/j.burns.2006.10.380>.
69. Herndon DN, Barrow RE, Stein M, Linares H, Rutan TC, Rutan R, et al. Increased mortality with intravenous supplemental feeding in severely burned patients. *J Burn Care Rehabil.* 1989;10(4):309–13.
70. Fuzaylov G, Fidkowski CW. Anesthetic considerations for major burn injury in pediatric patients. *Paediatr Anaesth.* 2009;19(3):202–11. <https://doi.org/10.1111/j.1460-9592.2009.02924.x>.