Burn Care and Treatment

A Practical Guide

Marc G. Jeschke
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Shahriar Shahrokhi
Editors

Second Edition

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Initial Assessment, Resuscitation, Wound Evaluation, and Early Care

Shahriar Shahrokhi

1 Initial Assessment and Emergency Treatment

The initial assessment and management of a burn patient begins with prehospital care. There is a great need for efficient and accurate assessment, transportation, and emergency care for these patients in order to improve their overall outcome. Once the initial evaluation has been completed, the transportation to the appropriate care facility is of outmost importance. At this juncture, it is imperative that the patient is transported to facility with the capacity to provide care for the thermally injured patient; however, at times patients would need to be transported to the nearest care facility for stabilization (i.e., airway control, establishment of IV access).

Once in the emergency room, the assessment as with any trauma patient is composed of primary and secondary surveys (Box 1). As part of the primary survey, the establishment of a secure airway is paramount. An expert in airway management should accomplish this as these patients can rapidly deteriorate from airway edema.

Even though, early and appropriate intubation is essential in the overall management of thermal injured patients, recent publication by Romanowski

Box 1 Primary and Secondary Survey

Primary survey:

- Airway:
  - Preferably #8 ETT placed orally.
  - Always be prepared for possible surgical airway.
- Breathing:
  - Ensure proper placement of ETT by auscultation/X-ray.
  - Bronchoscopic assessment for inhalation injury.
- Circulation:
  - Establish adequate IV access (large bore IV placed peripherally in non-burnt tissue if possible, central access would be required but can wait).
  - Begin resuscitation based on the Parkland formula.

Secondary survey:

- Complete head to toe assessment of patient.
- Obtain information about the patient's past medical history, mediations, allergies, tetanus status.
- Determine the circumstances/mechanism of injury.
  - Entrapment in closed space.
  - Loss of consciousness.
  - Time since injury.
  - Flame, scald, grease, chemical, electrical.

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- Examination should include a thorough neurological assessment.
- All extremities should be examined to determine possible neurovascular compromise (i.e. possible compartment syndrome) and need for escharotomies.
- Burn size and depth should be determined at the end of the survey.

(2016) demonstrated that one third of patients transferred to burn centers are unnecessarily intubated [1]. In addition, the study by Ching and colleagues (2014) demonstrated that the traditional findings of singed nasal hairs, carbonaceous sputum, and facial burns are unreliable evidence for inhalation injury. Thus, they concluded that these physical findings are not absolute indicators for intubation and should be interpreted as one component of the history and physical [2].

In order to determine those that would benefit from securing an airway via intubation, one needs to consider the following:

- Ability to protect their airway.
- GCS level.
- Presence of deep facial burns.
- Inhalation injury (history of enclosed space, loss of consciousness, presence of toxic fumes).
- Need for massive and ongoing resuscitation (typically reserved for TBSA >20–30%).

Once this initial assessment is complete, the disposition of the patient will be determined by the ABA criteria for burn center referral [3] (Table 1).

In determining the percent total body surface area (%TBSA) burn, the rule of nines or the palm method (the surface area of the patient's palm excluding the fingers = 0.5% TBSA) can be used; however, they are not as accurate as the Lund and Browder chart (Fig. 1). Attention must be paid to exclude superficial burns (First-degree burns) from the TBSA calculation.

Table 1 ABA criteria for referral to a burn center[a]

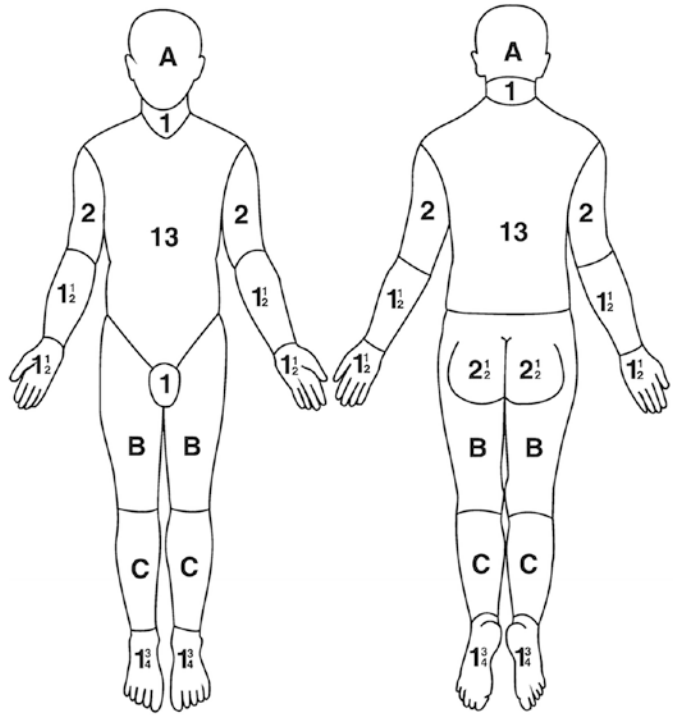
1.	Partial-thickness burns greater than 10% total body surface area (TBSA)
2.	Burns that involve the face, hands, feet, genitalia, perineum, or major joints
3.	Third-degree burns in any age group
4.	Electrical burns, including lightning injury
5.	Chemical burns
6.	Inhalation injury
7.	Burn injury in patients with preexisting medical disorders that could complicate management, prolong recovery, or affect mortality
8.	Any patient with burns and concomitant trauma (such as fractures) in which the burn injury poses the greatest risk of morbidity or mortality. In such cases, if the trauma poses the greater immediate risk, the patient may be initially stabilized in a trauma center before being transferred to a burn unit. Physician judgment will be necessary in such situations and should be in concert with the regional medical control plan and triage protocols
9.	Burned children in hospitals without qualified personnel or equipment for the care of children
10.	Burn injury in patients who will require special social, emotional, or rehabilitative intervention

[a]From Ref. [3]

More recently, the use of technology in the form three-dimensional software has proven to be more accurate than the conventional two-dimensional methods [4, 5].

Assessment of burn depth can be precarious even for experts in the field. There are some basics principles, which can help in evaluating the burn depth (Table 2). Always be aware that burns are dynamic and burn depth can progress or convert (due to a secondary insult) to becoming deeper. Therefore, frequent reassessment in the first 72 h is important in establishing burn depth.

Given that even burn experts are only 64–76% [6] accurate in determining burn depth, there has been an increased desire to have more objective method of determining burn depth, and therefore, technologies have been and continue to be developed and utilized in this field. Out of these various tools, laser doppler imaging (LDI) has garnered the most following. These are summarized in the following Table 3 [7]:



REGION	%
HEAD	
NECK	
ANT.TRUNK	
POST.TRUNK	
RIGHT ARM	
LEFT ARM	
BUTTOCKS	
GENITALIA	
RIGHT LEG	
LEFT LEG	
TOTAL BURN	

RELATIVE PERCENTAGE OF BODY SURFACE AREA AFFECTED BY GROWTH

AREA	AGE 0	1	5	10	15	ADULT
A = ½ OF HEAD	9½	8½	6½	5½	4½	3½
B = ½ OF ONE THIGH	2¾	3¼	4	4½	4½	4¾
C = ½ OF ONE LEG	2½	2½	2¾	3	3¼	3½

Fig. 1 Lund and Browder chart for calculating %TBSA burn

Table 2 Typical clinical appearance of burn depth

Superficial (first-degree) burns	Involves only the epidermis and never blisters
	Appears as a "sunburn"
	Is not included in the %TBSA calculation
Partial-thickness (second-degree) burns	Superficial
	Pink, homogeneous, normal cap refill, painful, moist, intact hair follicles
	Deep
	Mottled or white, delayed or absent cap refill, dry, decreased sensation or insensate, non-intact hair follicles
Full-thickness (third-degree) burns	Dry, white or charred, leathery, insensate

Once the initial assessment and stabilization are complete, the physician needs to determine the patient's disposition. Those that can be treated as outpatient (typically small, superficial, superficial partial-thickness burns in healthy individuals for whom outpatient care and suitable follow-up can be arranged) will need their wounds treated appropriately and discharged. There are many choices for outpatient wound therapy, and the choice will be mostly dependent on the availability of products and physician preference/knowledge/comfort with application. Table 5 summarizes some of the available products.

The thermally injured patients who are transferred to burn centers for treatment will be discussed in the next section on fluid resuscitation and early management.

Table 3 Techniques used for assessment of burn depth[a]

Technique	Advantages	Disadvantages
Radioactive isotopes	Radioactive phosphorus (^{32}P) taken up by the skin	Invasive, too cumbersome, poorly reproducible
Nonfluorescent dyes	Differentiate necrotic from living tissue on the surface	No determination of depth of necrosis; many dyes not approved for clinical use
Fluorescent dyes	Approved for clinical use	Invasive; marks necrosis at a fixed distance in millimeters, not accounting for thickness of the skin; large variability
Thermography	Noninvasive, fast assessment	Many false positives and false negatives based on evaporative cooling and presence of blisters; each center needs to validate its own values
Photometry	Portable, noninvasive, fast assessment, validated against senior burn surgeons, and color palette was developed	Single-institution experience; considered expensive technology
Liquid crystal film	Inexpensive	Contact with tissue required, unreliable readings
Nuclear magnetic resonance	Water content in tissue differentiates partial from full-thickness wounds	In vitro assessment only, expensive, time-consuming
Nuclear imaging	^{99}mTc shows areas of deeper injury	Expensive, very time-consuming, not readily available, and invasive
Pulse-echo ultrasound	Noninvasive, easily available	Underestimates depth of injury, operator-dependent, and requires contact with tissue
Doppler ultrasound	Noncontact technology available, provides morphologic and flow information	Operator-dependent, not as reliable as laser Doppler
Laser Doppler imaging	Noninvasive and noncontact technology, fast assessment, large body of experience in multiple centers, and very accurate prediction in small wounds in stable patients	Readings affected by temperature, distance from wound, wound humidity, angle of recordings, extent of tissue edema, and presence of shock; different versions of the technology available make extrapolation of results difficult

[a]From Jaskille et al. [7]

2 Fluid Resuscitation and Early Management

2.1 Fluid Resuscitation

As mentioned previously, patients with <10% TBSA burn do not require fluid resuscitation. However, burn encompassing >15% TBSA will require fluid resuscitation. Several formulas have been proposed for the resuscitation of the burn patient, all requiring crystalloid infusion with or without the addition of colloids. However, the mainstay of fluid resuscitation remains the Parkland formula:

$$4\,\text{ml} \times \%\,\text{TBSA} \times \text{weight}\,(\text{kg}) = 24\,\text{h Fluid requirements}$$

Half given in the first 8 h and the remainder over the following 16 h.

While the Parkland formula provides with the total amount for 24 h and starting level for initiation of resuscitation, it is not absolute. The fluid resuscitation should be guided by physiological parameters and laboratory findings to prevent under/over-resuscitation. The goals of resuscitation should be restoration of intravascular volume, maintenance of organ perfusion and function, while preventing burn wound conversion.

In resuscitating a thermally injured patient, one must be cognizant of the three components of burn shock: cardiogenic shock, distributive shock, and hypovolemic shock. Each has a fundamental role in the pathophysiology of the burn patient and cannot be treated in a similar fashion. The myocardial depressant effects of inflammatory mediators post-burn injury has been well documented [8–12]. This typically last up to 36 h following which the patients' cardiac function typically becomes hyper-dynamic.

Therefore, during the initial phase of burn resuscitation, the physician not only has to restore the patients' intravascular volume but also might need to consider inotropic agents to aid the myocardial dysfunction.

2.2 Endpoint of Burn Resuscitation

Traditionally, the endpoints of resuscitation of a thermally injured patient have been determined via physiological parameters; however, the use of global end-organ functions such as urinary output, heart rate, and blood pressure is inadequate in determining the adequacy of resuscitation [13]. The addition of measurements of base deficit and lactate has become commonplace as markers of adequate resuscitation; however, it is difficult to ascertain their importance as markers of burn resuscitation, as there are multiple episodes of ischemia and reperfusion injury which result in fluctuating levels of serum lactate and base deficit [14]. In some studies, it appears that elevated lactate and base deficit levels on admission do correlate with overall organ dysfunction and mortality; however, there is no absolute number or threshold, which determines non-survivability [15–18]. Moreover, further studies have concluded that elevated lactate level is an independent risk factor for mortality [19–21].

Since at this juncture, there is no ideal method for determining the endpoints of resuscitation, some researchers have begun to adopt new techniques. Light et al. demonstrated the use of tissue pCO_2 monitoring to better correlate with tissue perfusion; however, its use is not commonplace as yet [14]. Consideration should be given to use of dynamic echocardiography, pulse contour measurements, PiCCO monitor as adjuncts to overall physiological parameters for resuscitation [22–25].

Clinical assessment is outdated; the use of resuscitation markers (BD and lactate) is flawed; however, there are some which correlate well with overall risk of organ dysfunction and mortality. Newer techniques are under examination but have not gained wide acceptance for use. In conclusion, until a widely accepted method has been validated, care must be taken to incorporate as many tools as possible to determine adequate resuscitation.

2.3 Fluid Over-Resuscitation and Fluid Creep

The mainstay of fluid resuscitation remains crystalloid solutions (mainly Ringer's lactate). However, consideration should be given to colloids if the resuscitation volumes are far exceeding those set out by the Parkland calculation as not to endure the consequences of fluid creep [26] such as:

- Abdominal compartment syndrome (ACS) [26–30].
- Extremity compartment syndrome [31].
- Respiratory failure and prolonged intubation [32].
- Pulmonary edema and pleural effusions [32].
- Orbital compartment syndrome [33].

One of the more dire consequences of fluid creep is ACS, with resultant mortality of 70–100% [27–31, 34–37]. Some of the strategies that can be utilized to decrease risk of ACS or prevent intra-abdominal hypertension (IAH) progressing to ACS in a burn patient are:

- Vigilant monitoring of fluid resuscitation—decrease fluid volumes as quickly as possible.
- Monitor intra-abdominal pressures in all patients with ≥30% TBSA burn.
- Perform escharotomies on full-thickness torso burns and proceed to a "checkerboard pattern" if inadequate.
- Consider aggressive diuresis if evidence of over-resuscitation.
- Consider neuromuscular blockade to alleviate abdominal muscle tone.

Should all the above strategies fail in lowering the intra-abdominal pressure, the definitive solution is a decompressive laparotomy with aforementioned mortality of up to 100% [27–31, 34–37]. As a result, many have looked at other modes of resuscitation beyond the use of crystalloid solutions.

2.4 Role of Colloids, Hypertonic Saline, and Antioxidants in Resuscitation

2.4.1 Colloids

As mentioned previously, the initial resuscitation is accomplished with mainly crystalloids. This is mainly as the consequence of burn pathophysiology, whereby there is a significant increase in the permeability of capillaries post-thermal injury with resultant shift of fluid into the interstitial space [38–43]. This increase permeability appears to resolve in 8–12 h post-injury. Typically, colloids are not recommended in the initial 12 h phase of resuscitation (however, there is no clear evidence as to the exact timing for initiation of colloids).

The colloid of choice has typically been albumin (5% concentration), given as an infusion to decrease the crystalloid requirements. There is some evidence that use of colloids in the resuscitation of the thermally injured patient does normalize the I/O ratios; however, the effect on morbidity and mortality is unknown at this time [44, 45]. In critical care literature, which typically excludes the burn patients, the studies have shown that the use of colloids is safe with no overall benefit to the patient [46], and the Cochrane review in 2011 concluded that "there is no evidence that albumin reduces mortality in patients with hypovolemia, burns or hypoproteinemia. For patients with burns or hypoproteinemia, there is a suggestion that albumin administration may increase mortality" [47]. More recent meta-analysis by Navickis and colleagues (2016) concluded that "the optimal timing, dose, and patient population for albumin use remains unclear" [48]. This meta-analysis demonstrated that the scope and quality of available evidence is limited, and new multicenter clinical trials should be conducted [48]. Therefore, despite the extensive of use of albumin in burn resuscitation, there is paucity of high-quality evidence for its use, and the overall benefit remains controversial.

2.4.2 Hypertonic Saline

The role of hypertonic saline in burn resuscitation has been studied greatly with variable results. In recent years, there has been a shift in thinking in the use of hypertonic saline. Rather than using hypertonic saline as the sole resuscitative fluid with goals of reducing fluid requirements, it has been studied in the context of decreasing the inflammatory response and bacterial translocation and therefore infectious complications [49–51].

2.4.3 Antioxidants: High-Dose Vitamin C

It is well documented that following thermal injury, there is an increase in capillary permeability leading to edema. The initial studies conducted by Tanaka et al. and Matsuda et al. indicated the lower water content of burn wounds with high-dose vitamin C infusion, with

Table 4 Clinical appearance of dermal and full-thickness burns

Clinical appearance	Superficial partial-thickness	Deep partial-thickness	Full-thickness
Presence of blisters	Yes	Yes	No
Dermal depth	Papillary	Reticular	Entire depth
Color of exposed dermis	Pink	Mottled/white	White/charred/leathery
Capillary refill	Yes	Delayed/none	None
Time to heal	<21 days	>21 days	>21 days
Moisture	Moist	Dry	Dry
Pain	Very painful	Minimal to none	Insensate
Dermal appendages	Intact	Not intact	Not intact

decreased overall resuscitation fluid requirements [52–55]. More recently, studies have demonstrated that resuscitation with high-dose vitamin C reduces the endothelial damage post-thermal injury [56, 57], with decrease in overall fluid volumes administered with no increase in morbidity or mortality [57, 58].

In summary, the resuscitation of the burn patient is complex and requires the use of all tools available. It can no longer be the domain of crystalloid resuscitation without consideration for colloids, hypertonic saline, and high-dose vitamin C along with other antioxidants. All aspects of burn shock require treatment (not just the hypovolemic component), which might require the early use of vasopressors and inotropes. Finally, the end goals of resuscitation need to be better monitored to assess the effectiveness of the resuscitation and ensure improved patient outcomes.

3 Evaluation and Early Management of Burn Wound

3.1 Evaluation of Burn Depth

The evaluation of the burn wound is of utmost importance, and expert clinicians have been known to be incorrect in their assessment up to 30% of the time. As previously indicated, multiple modalities have been examined to determine their efficacy and possible role in the determination of the burn depth (Table 3), but none has replaced the clinical examination as gold standard.

In general, superficial (first-degree) burns are of minimal concern. They only involve the epidermis with erythema and no blisters and do not require medical attention. Partial-thickness (second-degree) burns and beyond are those that will require medical attention. Partial-thickness burns are divided into superficial and deep. Their clinical characteristics are summarized in Table 4.

The depth of the burn determines not only the requirement for admission but also the management—operative versus conservative. The ideal treatment for all burns, which will not heal between 14 and 21 days, is to have operative excision and skin grafting. All others can be treated conservatively. The conservative management of burns includes appropriate wound care and therapy for maintenance of range of motion and overall function.

3.2 Choice of Topical Dressings

There are various topical agents that are available for management of burns. Typically, the topical management of deep burns requires an antimicrobial agent to minimize bacterial colonization and hence infection. For superficial burns, the goal of the topical agent is to reduce environmental factors causing pain and provide the appropriate environment for wound healing. Table 5 summarizes some of the agents available for topical treatment of burns, and the choice of agent is dependent on their availability and the comfort and knowledge of the caregivers.

The choice of burn dressing needs to take into account the following factors:

Table 5 Topical therapy for treatment of cutaneous burns

Agent	Description
Topical ointments for small superficial burns	
Bacitracin/ polymyxin B	Ointment for superficial burns
Mupirocin	2% ointment for superficial partial-thickness burns
	Activity against MRSA [59]
Topical antiseptics and antimicrobials	
Mafenide acetate	Available as 11% water-soluble cream or 5% solution
	Has broad spectrum of activity, but poor antifungal activity
	Excellent eschar penetration Cytotoxic to fibroblasts and keratinocytes [60–62] Consider for deep dermal and full-thickness burns 11% cream for deep ear burn to prevent suppurative chondritis [63]
Sodium hypochlorite	Various concentrations (0.005–0.5%) Extensive spectrum of activity against bacteria, fungi, and viruses Can disrupt biofilm [64] At higher concentrations is cytotoxic to fibroblasts and keratinocytes [60] Consider in deep/full-thickness burns prior to debridement or heavily contaminated wounds and those with biofilm
Acetic acid	Solution of 3% is bactericidal against broad range of pathogens [65] Solution of 2.5% can eradicate biofilm formation [66] Solution >0.25% can inhibit fibroblasts and keratinocytes [61] Potential role in infected wounds and those with biofilm
Silver containing topical agents and dressings	
Aquacel® *Ag*	Methylcellulose dressing with ionic silver for partial-thickness burns
	Can be left intact until wound fully healed Has comparable efficacy to Acticoat in healing time and antimicrobial activity [67]
Silver sulfadiazine	1% cream for deep dermal and full-thickness burns
	Has broad spectrum of activity
	Intermediate eschar penetration and short duration of activity Can form a pseudo eschar and is cytotoxic to fibroblasts and keratinocytes [68–71]
Acticoat™	Nanocrystalline silver dressing that can be left on the wound from 3 to 7 days Has broad spectrum of activity [72, 73] As with all silver containing topical products can inhibit fibroblasts and keratinocytes Preferred for deep dermal/ full-thickness burn wounds with higher risk of infection

- Eliminate the environmental factors causing pain.
- Act as barrier to environmental flora.
- Reduce evaporative losses.
- Absorb and contain drainage.
- Provide splinting to maintain position of function.
- Should not retard wound healing.

The goals of topical antimicrobial therapy for deep dermal and full-thickness burns:

- To delay/minimize wound colonization.
- Have the ability to penetrate eschar.
- Have activity against common pathogens.
  - *S. aureus, Proteus, Klebsiella, E. coli, Pseudomonas.*
- Have low toxicity (minimal systemic absorption).

3.3 Escharotomy

In evaluation of wounds, consideration also needs to be given for possible need for escharotomy (Fig. 2). All deep circumferential burns to the extremity have the potential to cause neurovascular compromise and therefore benefit from escharotomies. The typical clinical signs of impaired

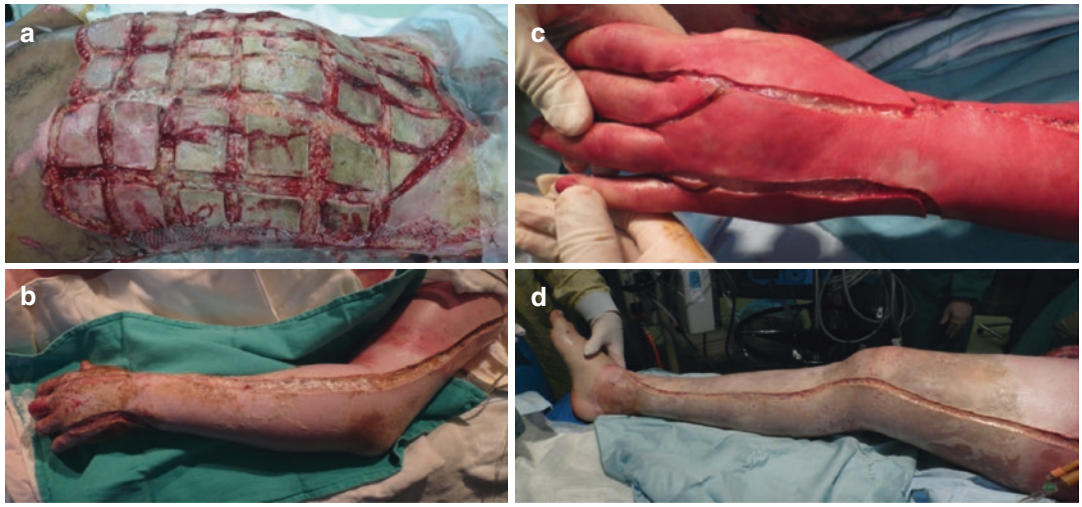


Fig. 2 Examples of escharotomies: (**a**) Checkerboard escharotomy of abdomen (**b**) escharotomy of the arm along medial lateral line (**c**) escharotomy of the hand between the second and third and fourth and fifth metacarpal bones (**d**) escharotomy of the leg along the medial and lateral lines

perfusion in the burned extremity/hand include cool temperature, decreased or absent capillary refill, tense compartments, with the hand held in the claw position, and the absence of pulses is a late sign [74]. On occasion, non-circumferential deep burns or circumferential partial-thickness burns might require a prophylactic escharotomy as the patient might require large resuscitation volumes due to overall injury or the inability to perform serial reassessments [74].

Escharotomies of the extremities are performed along the medial and lateral lines, with the extremity held in the anatomic position. For the hand, the escharotomy is performed along the second and fourth metacarpals, and for the fingers, care is taken to prevent any injury to the neurovascular bundle; therefore, escharotomies are typically not performed along the ulnar aspect of the thumb or the radial aspect of the index finger [74–76].

3.4 Operative Management

Once the thermally injured patient has been admitted, resuscitated, all wounds assessed, and managed appropriately with escharotomy and appropriate topical dressings, the surgeon needs to determine the most efficient course of action in regard to excision of burn and coverage. This needs to be undertaken as soon as the patient is fully resuscitated, usually within 72 h post-injury.

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Pathophysiology of Burn Injury

Marc G. Jeschke

1 Introduction

Advances in therapy strategies, due to improved understanding of resuscitation, enhanced wound coverage, better support of hypermetabolic response to injury, more appropriate infection control and improved treatment of inhalation injury, based on better understanding of the pathophysiologic responses after burn injury have further improved the clinical outcome of this unique patient population over the past years [1]. This chapter describes the present understanding of the pathophysiology of a burn injury including both the local and systemic responses, focusing on the many facets of organ and systemic effects directly resulting from hypovolemia and circulating mediators following burn trauma.

2 Local Changes

2.1 Temperature and Time Effect

Local changes appear in the tissue when the amount of absorbed heat exceeds the body system's compensatory mechanisms. On a molecular level, protein degradation begins at a temperature of 40 °C. This degradation leads to alterations in cell homeostasis. This is reversible if the temperature is lowered. Starting at 45 °C proteins are permanently denatured. This is reflected by local tissue necrosis. The speed with which permanent tissue damage can appear is dependent on time exposed and temperature (Table 1).

Table 1 Time and temperature exposure to cause a burn injury

45–51 °C	Within minutes
51 und 70 °C	Within seconds
Above 70 °C	Less than a second

The depth and severity of the burn are also determined by the ability of the contact material to transfer heat, a factor referred to as the specific heat. This is especially important in scald and contact burns. The knowledge about the material type allows for a more accurate estimate of tissue damage.

Definition: Burn depth is determined by the time of exposure, the temperature at which the burn occurred, and the caloric equivalent of the burn media.

Another determinant of the severity of burn is the location of the burn wound and the age of the burn patient. The thickness of the skin layers increases from the age of 5 up to the age of 50. In elderly patients, the thickness starts to decrease at the age of 65. The epidermis can vary by location from 0.03 up to 0.4 mm. Clinically, the severity of burn injury can be categorized by the differ-

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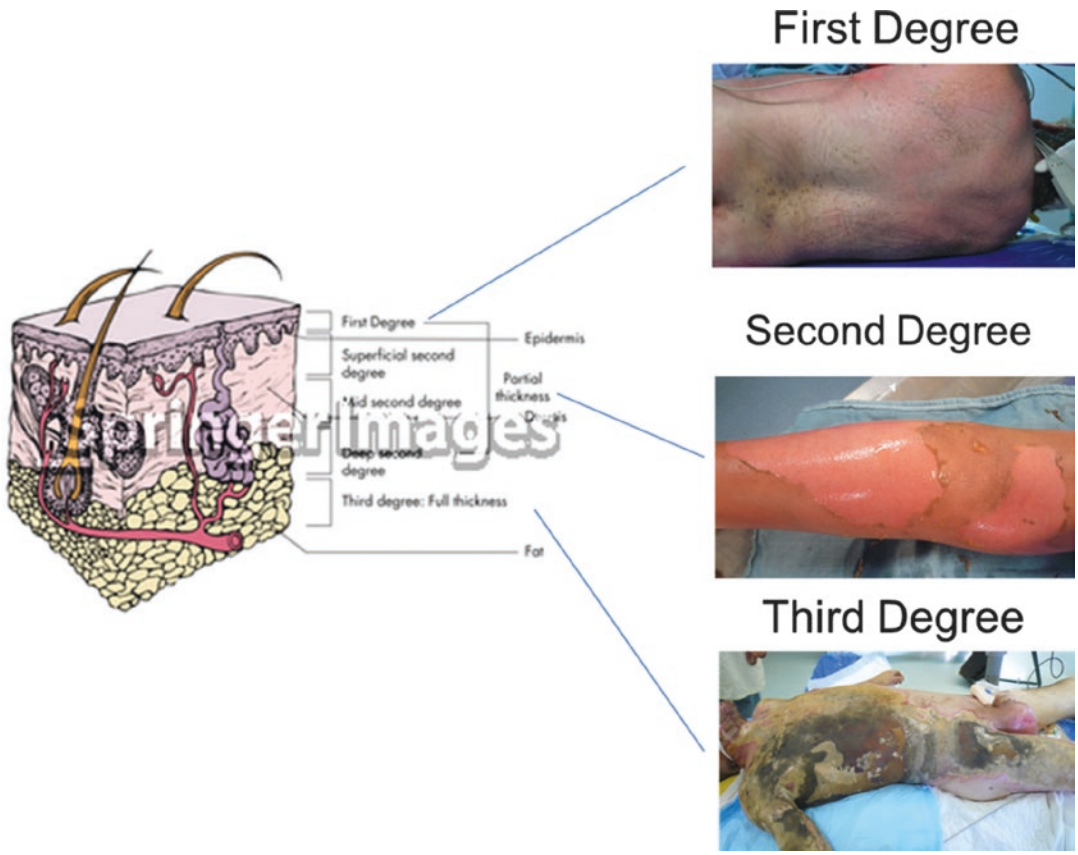

Fig. 1 Burn depth estimation based on appearance

ences in the tissue damage and is determined by the depth of the burn (Fig. 1).

1. **I degree: Superficial burn of the epidermis**
   First-degree burns are painful, erythematous, and blanch to the touch with an intact epidermal barrier. Examples include sunburn or a minor scald from a kitchen accident. These burns do not result in scarring, and treatment is aimed at comfort with the use of topical soothing salves with or without aloe and oral nonsteroidal anti-inflammatory agents.
2. **IIa degree: Burn including epidermis and superficial dermis**
3. **IIb degree: Burn including epidermis and deep dermis**
   Second-degree burns are divided into two types: superficial and deep. All second-degree burns have some degree of dermal damage, by definition, and the division is based on the depth of injury into the dermis. Superficial dermal burns are erythematous, painful, blanch to touch, and often blister. Examples include scald injuries from overheated bathtub water and flash flame burns. These wounds spontaneously re-epithelialize from retained epidermal structures in the rete ridges, hair follicles, and sweat glands in 1–2 weeks. After healing, these burns may have some slight skin discoloration over the long term. Deep dermal burns into the reticular dermis appear more pale and mottled, do not blanch to touch, but remain painful to pinprick. These burns heal in 2–5 weeks by re-epithelialization from hair follicles and sweat gland keratinocytes, often with severe scarring as a result of the loss of dermis.
4. **III degree: Burn including epidermis and dermis and subcuticular layer**
   Third-degree burns are full thickness through the epidermis and dermis and are characterized by a hard, leathery eschar that is

painless and black, white, or cherry red. No epidermal or dermal appendages remain; thus, these wounds must heal by re-epithelialization from the wound edges. Deep dermal and full-thickness burns require excision with skin grafting from the patient to heal the wounds in a timely fashion.

5. **IV degree: All dermal layers including fascia, muscles, and/or bones**

   Fourth-degree burns involve other organs beneath the skin, such as muscle, bone, and brain.

Currently, burn depth is most accurately assessed by judgment of experienced practitioners. Accurate depth determination is critical to wound healing as wounds that will heal with local treatment are treated differently than those requiring operative intervention. Examination of the entire wound by the physicians ultimately responsible for their management then is the gold standard used to guide further treatment decisions. New technologies, such as the multi-sensor laser Doppler flow meter, hold promise for quantitatively determining burn depth.

2.2 Etiology

The causes include injury from flame (fire), hot liquids (scald), contact with hot or cold objects, chemical exposure, and/or conduction of electricity. The first three induce cellular damage by the transfer of energy, which induces a coagulation necrosis. Chemical burns and electrical burns cause direct injury to cellular membranes in addition to the transfer of heat.

2.3 Pathophysiologic Changes

The area of cutaneous or superficial injury has been divided into three zones: zone of coagulation, zone of stasis, and zone of hyperemia. The necrotic area of burn where cells have been disrupted is termed the *zone of coagulation*. This tissue is irreversibly damaged at the time of injury.

The area immediately surrounding the necrotic zone has a moderate degree of insult with decreased tissue perfusion. This is termed the *zone of stasis* and, depending on the wound environment, can either survive or go on to coagulation necrosis. The zone of stasis is associated with vascular damage and vessel leakage [2, 3]. This area is of great importance as this area determines the injury depth of the burned skin. It is important to note that over-resuscitation and increased edema formation can increase the depth of burn and hence the zone of coagulation and fluids should not only be restricted to avoid pulmonary edema and abdominal compartment syndromes but also to minimize the progressive damage to the burned skin. Other means to attenuate the damage and prevent progression are antioxidants, bradykinin antagonists, and negative wound pressures also improve blood flow and affect the depth of injury [4–6]. Local endothelial interactions with neutrophils mediate some of the local inflammatory responses associated with the zone of stasis. Treatment directed at the control of local inflammation immediately after injury may spare the zone of stasis.

The last area is the *zone of hyperemia,* which is characterized by vasodilation from inflammation surrounding the burn wound. This region contains the clearly viable tissue from which the healing process begins and is generally not at risk for further necrosis.

2.4 Burn Size

Determination of burn size estimates the extent of injury. Burn size is generally assessed by the "rule of nines" (Fig. 2). In adults, each upper extremity and the head and neck are 9% of the TBSA, the lower extremities and the anterior and posterior trunk are 18% each, and the perineum and genitalia are assumed to be 1% of the TBSA. Another method of estimating smaller burns is to equate the area of the open hand (including the palm and the extended fingers) of the patient to be approximately 1% TBSA and then to transpose that measurement visually onto the wound for a determination of its size. This method is crucial when evaluating burns of mixed distribution. Children have a relatively larger portion of the body surface area in the head and

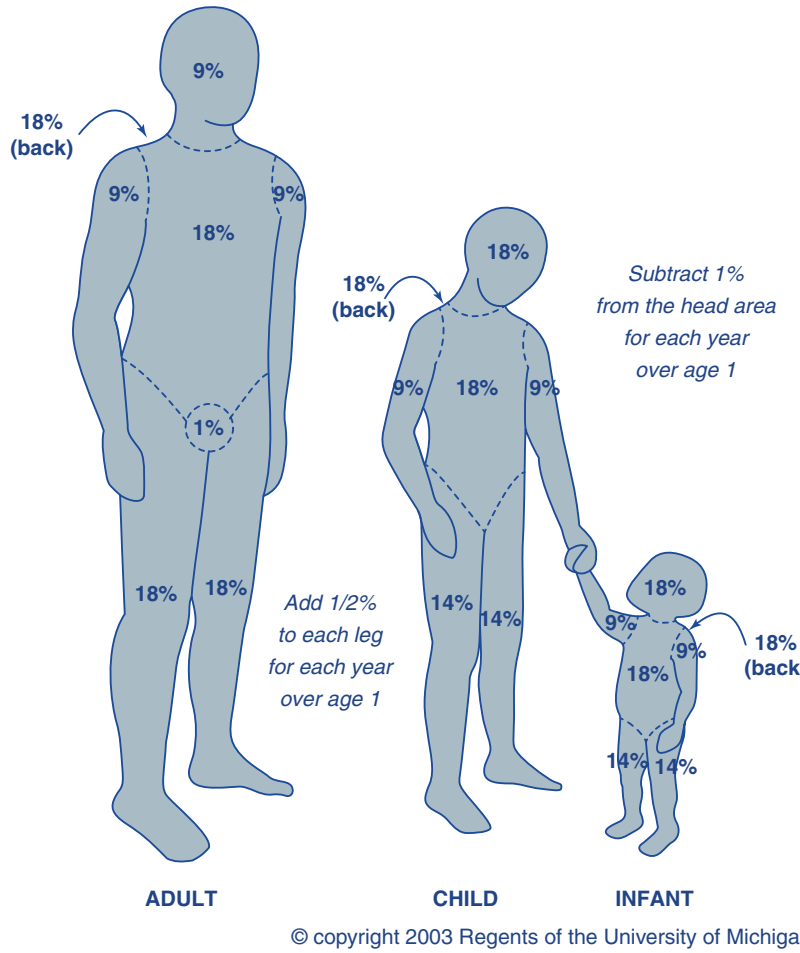

Fig. 2 Burn size estimation Lund Browder or rules of nines for adult patient and the Berkow formula for children

neck, which is compensated for by a relatively smaller surface area in the lower extremities. Infants have 21% of the TBSA in the head and neck and 13% in each leg, which incrementally approaches the adult proportions with increasing age. The Berkow formula is used to accurately determine burn size in children (Fig. 2).

3 Systemic Changes

3.1 Edema Formation

The release of cytokines and other inflammatory mediators at the site of injury has a systemic effect once the burn reaches 20–30% of total body surface area (TBSA) resulting in the severe and unique derangements of cardiovascular function called burn shock. Burn shock is a complex process of circulatory and microcirculatory dysfunction that is not easily or fully repaired by fluid resuscitation. Severe burn injury results in significant hypovolemic shock and substantial tissue trauma, both of which cause the formation and release of many local and systemic mediators [1, 7, 8]. Burn shock results from the interplay of hypovolemia and the release of multiple mediators of inflammation with effects on both the microcirculation and the function of the heart, large vessels, and lungs. Subsequently, burn shock continues as a significant pathophysiologic state, even if hypovolemia is corrected. Increases in pulmonary and systemic vascular resistance (SVR) and myocardial depression occur despite adequate preload and volume support [9–12]. Such cardiovascular dysfunctions can further

exacerbate the whole-body inflammatory response into a vicious cycle of accelerating organ dysfunction [1, 9–12].

Burn injury causes extravasation of plasma into the burn wound and the surrounding tissues. Extensive burn injuries are hypovolemic in nature and characterized by the hemodynamic changes similar to those that occur after hemorrhage, including decreased plasma volume, cardiac output, urine output, and an increased systemic vascular resistance with resultant reduced peripheral blood flow [1, 9–12]. However, as opposed to a fall in hematocrit with hemorrhagic hypovolemia due to transcapillary refill an increase in hematocrit and hemoglobin concentration will often appear even with adequate fluid resuscitation. As in the treatment of other forms of hypovolemic shock, the primary initial therapeutic goal is to quickly restore vascular volume and to preserve tissue perfusion in order to minimize tissue ischemia. In extensive burns (>20–30%TBSA), fluid resuscitation is complicated not only by the severe burn wound edema, but also by extravasated and sequestered fluid and protein in non-burned soft tissue. Large volumes of resuscitation solutions are required to maintain vascular volume during the first several hours after an extensive burn. Data suggests that despite fluid resuscitation normal blood volume is not restored until 24–48 h after large burns.

Edema develops when the rate by which fluid is filtered out of the microvessels exceeds the flow in the lymph vessels draining the same tissue mass. Edema formation often follows a biphasic pattern. An immediate and rapid increase in the water content of burn tissue is seen in the first hour after burn injury [13–15]. A second and more gradual increase in fluid flux of both the burned skin and non-burned soft tissue occurs during the first 12–24 h following burn trauma. The amount of edema formation in burned skin depends on the type and extent of injury and whether fluid resuscitation is provided as well as the type and volume of fluid administered. However, fluid resuscitation elevates blood flow and capillary pressure contributing to further fluid extravasation [14, 15]. Without sustained delivery of fluid into the circulation edema fluid is somewhat self-limited as plasma volume and capillary pressure decrease. The edema development in thermal injured skin is characterized by the extreme rapid onset of tissue water content, which can double within the first hour after burn [14, 15]. Leape and colleagues found a 70–80% water content increase in a full-thickness burn wound 30 min after burn injury with 90% of this change occurring in the first 5 min [16]. There was little increase in burn wound water content after the first hour in the non-resuscitated animals. In resuscitated animals or animals with small wounds, adequate tissue perfusion continues to "feed" the edema for several hours. Demling and others used dichromatic absorptionmetry to measure edema development during the first week after an experimental partial-thickness burn injury on one hind limb in sheep [14]. Even though edema was rapid with over 50% occurring in the first hour, maximum water content did not occur until 12–24 h after burn injury.

3.2 Hemodynamic and Cardiac Changes Post-Burn

The cause of reduced cardiac output (CO) during the resuscitative phase of burn injury has been the subject of considerable debate. There is an immediate depression of cardiac output before any detectable reduction in plasma volume [9, 10]. The rapidity of this response suggests a neurogenic response to receptors in the thermally injured skin or increased circulating vasoconstrictor mediators. Soon after injury, a developing hypovolemia and reduced venous return undeniably contribute to the reduced cardiac output. The subsequent persistence of reduced CO after apparently adequate fluid therapy, as evidenced by a reduction in heart rate and restoration of both arterial blood pressure and urinary output, has been attributed to circulating myocardial depressant factor(s), which possibly originates from the burn wound. Demling and colleagues showed a 15% reduction in CO despite an aggressive volume replacement protocol after a 40% scald burn in sheep [15]. However, there are also sustained increases in catecholamine secretion

and elevated systemic vascular resistance for up to 5 days after burn injury [12, 17]. We recently conducted two clinical studies measuring CO and SVR in severely burned patients and showed that CO fell shortly after injury and then returned toward normal; however, reduced CO did not parallel the blood volume deficit [9, 10]. We concluded that the depression of CO resulted not only from decreased blood volume and venous return, but also from an increased SVR. Thus, there are multiple factors that can significantly reduce CO after burn injury. However, resuscitated patients suffering major burn injury can also have supranormal CO from 2 to 6 days post-injury. This is secondary to the establishment of a hypermetabolic state [9, 10].

Immediately post-burn patients have low cardiac output characteristic of early shock [18] However, 3–4 days post-burn, cardiac outputs are greater than 1.5 times that of non-burned, healthy volunteers [9–11]. Heart rates of pediatric burn patients' approach 1.6 times that of non-burned, healthy volunteers. Post-burn, patients have increased cardiac work [19, 20]. Myocardial oxygen consumption surpasses that of marathon runners and is sustained well into rehabilitative period [19, 21].

Myocardial function can be compromised after burn injury due to overload of the right heart and direct depression of contractility. Increases in the afterload of both the left and right heart result from SVR and PVR elevations. The left ventricle compensates and CO can be maintained with increased afterload by augmented adrenergic stimulation and increased myocardial oxygen extraction. Burn injury greater than 30% TBSA can induce intrinsic contractile defects that cannot be corrected by early and adequate fluid resuscitation [22, 23]. Horton also showed more recently that also the left heart can suffer from contractile dysfunction in isolated, coronary perfused, guinea pig hearts harvested 24 h after burn injury [22]. This dysfunction was more pronounced in hearts from aged animals and was not reversed by resuscitation with isotonic fluid. It was largely reversed by treatment with 4 ml/kg of hypertonic saline dextran (HSD), but only if administered during the initial 4–6 h of resuscitation. The authors also effectively ameliorated the cardiac dysfunction of thermal injury with infusions of antioxidants, arginine, and calcium channel blockers [23]. Various other resuscitation and cardiac function studies emphasize the importance of early and adequate fluid therapy and suggest that functional myocardial depression after burn injury maybe alleviated in patients receiving early and adequate volume therapy.

A recent more study delineated the importance of intact cardiac function. The authors compared various burn sizes and the pathophysiologic differences between the burn sizes. They found that the patient with larger burns showed significant worse cardiac function which was the only significant difference in terms of organ function indicating that the heart plays an important role and that cardiac dysfunction is present in large burns and should be accounted for [24].

We therefore suggest to use Dobutamine for impaired cardiac function, beta blocker for tachycardia and catecholamine blockade, and adequate resuscitation and hemoglobin levels.

3.3 Hypermetabolic Response Post-Burn

Marked and sustained increases in catecholamine, glucocorticoid, glucagon, and dopamine secretion are thought to initiate the cascade of events leading to the acute hypermetabolic stress response with its ensuing catabolic state [25–34]. The cause of this complex response is not well understood. However, cytokines, endotoxin, reactive oxygen species, nitric oxide, and coagulation as well as complement cascades have also been implicated in regulating this response to burn injury [35]. Once these cascades are initiated, their mediators and by-products appear to stimulate the persistent and increased metabolic rate associated with altered glucose, protein, and lipid metabolism seen after severe burn injury [36]. Several studies have indicated that these metabolic phenomena post-burn occur in a timely manner, suggesting two distinct pattern of metabolic regulation following injury [37].

The first phase occurs within the first 48 h of injury and has classically been called the "ebb phase" [18, 37], characterized by decreases in cardiac output, oxygen consumption, and metabolic rate as well as impaired glucose tolerance associated with its hyperglycemic state. These metabolic variables gradually increase within the first 5 days post-injury to a plateau phase (called the "flow" phase), characteristically associated with hyperdynamic circulation and the above-mentioned hypermetabolic state. Insulin release during this time period was found to be twice that of controls in response to glucose load [38, 39] and plasma glucose levels are markedly elevated, indicating the development of an insulin resistance [40, 41]. Current understanding has been that these metabolic alterations resolve soon after complete wound closure. However, we found in recent studies that sustained hypermetabolic alterations post-burn, indicated by persistent elevations of total urine cortisol levels, serum cytokines, catecholamines, and basal energy requirements, were accompanied by impaired glucose metabolism and insulin sensitivity that persisted for up to 3 years after the initial burn injury [42].

3.3.1 Resting Energy Expenditure

For severely burned patients, the resting metabolic rate at thermal neutral temperature (30 °C) exceeds 140% of normal at admission, reduces to 130% once the wounds are fully healed, then to 120% at 6 months after injury, and 110% at 12–36 months post-burn [1, 25, 43, 44]. Increases in catabolism result in loss of total body protein, decreased immune defenses, and decreased wound healing [45].

3.3.2 Muscle Catabolism

Post-burn, muscle protein is degraded much faster than it is synthesized. Net protein loss leads to loss of lean body mass and severe muscle wasting leading to decreased strength and failure to fully rehabilitate [20, 45, 46]. Significant decreases in lean body mass related to chronic illness or hypermetabolism can have dire consequences.

- 10% loss of lean body mass is associated with immune dysfunction.
- 20% loss of lean body mass positively correlates with decreased wound healing.
- 30% loss of lean body mass leads to increased risk for pneumonia and pressure sores
- 40% loss of lean body mass can lead to death [47].

Uncomplicated severely burned patients can lose up to 25% of total body mass after acute burn injury [48] and protein degradation persists up to 2–3 years post severe burn injury resulting in significant negative whole-body and cross-leg nitrogen balance [20, 45, 49]. Protein catabolism has a positive correlation with increases in metabolic rates (Fig. 3) [45]. Severely burned patients have a daily nitrogen loss of 20–25 g/m^2 of burned skin [20, 45, 46]. At this rate, a lethal cachexia can be reached in less than 1 month. Burned pediatric patients' protein loss leads to significant developmental delay for up to 24–36 months post-injury [44].

Severe burn causes marked changes in body composition during acute hospitalization. Severely burned children lost about 2% of their body weight (−5% LBM, −3% BMC, and −2% BMD) from admission to discharge. Total fat and percent fat increased from admission to discharge by 3% and 7%, respectively.

Septic patients have a particularly profound increase in metabolic rates and protein catabolism up to 40% more compared to those with like-size burns that do not develop sepsis [45]. A vicious cycle develops, as patients that are catabolic are more susceptible to sepsis due to changes in immune function and immune response. Modulation of the hypermetabolic, hypercatabolic response, thus preventing secondary injury is paramount in the restoration of structure and function of severely burned patients.

3.3.3 Glucose and Lipid Metabolism

Elevated circulating levels of catecholamines, glucagon, cortisol after severe thermal injury stimulate free fatty acids and glycerol from fat, glucose production by the liver, and amino acids

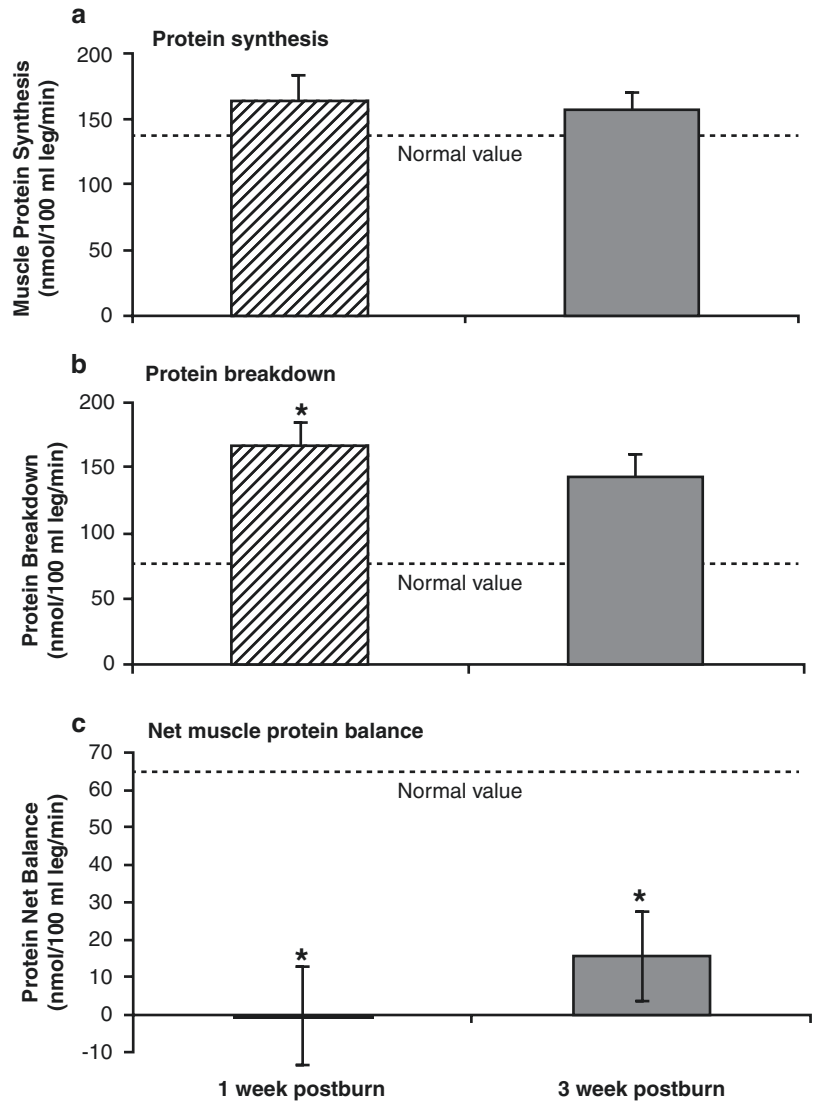

Fig. 3 Muscle protein synthesis, breakdown, and balance after burn injury. Burn causes substantial muscle protein breakdown with a minimal increase in synthesis leading to an overall substantial net protein balance

from muscle [37, 50, 51]. Specifically, glycolytic-gluconeogenic cycling is increased 250% during the post-burn hypermetabolic response coupled with an increase of 450% in triglyceride-fatty acid cycling [52]. These changes lead to increased lipolysis, fatty infiltration in various organs, hyperglycemia and impaired insulin sensitivity related to post-receptor insulin resistance and significant reductions in glucose clearance [17, 42, 53, 54].

In critical illness, metabolic alterations cause significant changes in energy substrate metabolism. In order to provide glucose, a major fuel source to vital organs, release of the above-mentioned stress mediators oppose the anabolic actions of insulin [55]. By enhancing adipose tissue lipolysis [51] and skeletal muscle proteolysis [56], they increase gluconeogenic substrates, including glycerol, alanine, and lactate, thus augmenting hepatic glucose production in burned patients [57–59]. Hyperglycemia fails to suppress hepatic glucose release during this time [60] and the suppressive effect of insulin on hepatic glucose release is attenuated, signifi-

cantly contributing to post-trauma hyperglycemia [61]. Catecholamine-mediated enhancement of hepatic glycogenolysis, as well as direct sympathetic stimulation of glycogen breakdown, can further aggravate the hyperglycemia in response to stress [57]. Catecholamines have also been shown to impair glucose disposal via alterations of the insulin signaling pathway and GLUT-4 translocation muscle and adipose tissue, resulting in peripheral insulin resistance [58, 62].

3.4 Renal System

Diminished blood volume and cardiac output result in decreased renal blood flow and glomerular filtration rate. Other stress-induced hormones and mediators such as angiotensin, aldosterone, and vasopressin further reduce renal blood flow immediately after the injury. These effects result in oliguria, which, if left untreated will cause acute tubular necrosis and renal failure. Twenty years ago, acute renal failure in burn injuries was almost always fatal. Today, newer techniques in dialysis became widely used to support the kidneys during recovery. The latest reports indicate an 88% mortality rate for severely burned adults and a 56% mortality rate for severely burned children in whom renal failure develops in the post-burn period [63, 64]. Early resuscitation decreases risks of renal failure and improves the associated morbidity and mortality [65].

If dialysis is needed, there are various approaches:

- Pediatric patients peritoneal dialysis (Tenckhoff catheter).
- Adult patients hemofiltration or hemodialysis.

We recommend using the dialysis form that is present in the individual setup.

The use of diuretics has been discussed controversially, but there seems to be strong support for the use of diuretics such as Lasix for patients being over-resuscitated, renal protection, or pulmonary edema.

3.5 Gastrointestinal System

The gastrointestinal response to burn is highlighted by mucosal atrophy, changes in digestive absorption, and increased intestinal permeability [66]. Atrophy of the small bowel mucosa occurs within 12 h of injury in proportion to the burn size and is related to increased epithelial cell death by apoptosis [66]. The cytoskeleton of the mucosal brush border undergoes atrophic changes associated with vesiculation of microvilli and disruption of the terminal web actin filaments. These findings were most pronounced 18 h after injury, which suggests that changes in the cytoskeleton, such as those associated with cell death by apoptosis, are processes involved in the changed gut mucosa [66]. Burn also causes reduced uptake of glucose and amino acids, decreased absorption of fatty acids, and reduction in brush border lipase activity. These changes peak in the first several hours after burn and return to normal at 48–72 h after injury, a timing that parallels mucosal atrophy.

Intestinal permeability to macromolecules, which are normally repelled by an intact mucosal barrier, increases after burn [67, 68]. Intestinal permeability to polyethylene glycol, lactulose, and mannitol increases after injury, correlating to the extent of the burn. Gut permeability increases even further when burn wounds become infected. A study using fluorescent dextrans showed that larger molecules appeared to cross the mucosa between the cells, whereas the smaller molecules traversed the mucosa through the epithelial cells, presumably by pinocytosis and vesiculation. Mucosal permeability also paralleled increases in gut epithelial apoptosis.

The best treatment to alleviate mucosal atrophy is early initiation of enteral nutrition, usually within 8–12 h post-burn. Glutamine and other antioxidants have been shown to improve enteral inflammatory driven pathways as well as gut function.

Despite the need for liver function and integrity the liver is profoundly affected post-burn and in our opinion a central contributor to post-burn morbidity and mortality [69–71]. The liver has

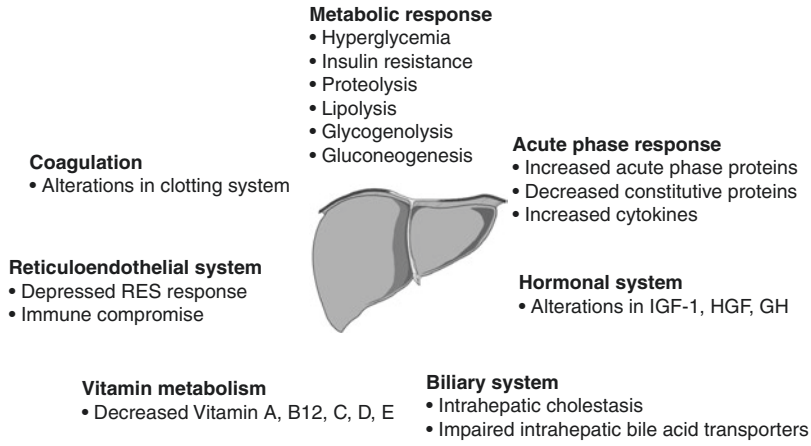

Fig. 4 Plethora of essential and physiologic functions of the liver under normal conditions and after burn

several myriad functions that are each essential for survival (Fig. 4):

All of these hepatic functions are affected by a thermal injury, and we have strong evidence that hepatic biomarkers predict and determine morbidity and mortality in severely burned patients. We, therefore, believe that the liver is central for post-burn outcome and we propose that attenuation of liver damage and restoration of liver function will improve morbidity and mortality of severely burned patients [69–71].

There is currently no treatment for hepatic dysfunction or failure post-burn. Animal and in vitro studies suggested a beneficial effect on hepatic apoptosis and function with the use of insulin and Propranolol.

3.6 Immune System

Burns cause a global depression in immune function, which is shown by prolonged allograft skin survival on burn wounds. Burned patients are then at great risk for a number of infectious complications, including bacterial wound infection, pneumonia, and fungal and viral infections. These susceptibilities and conditions are based on depressed cellular function in all parts of the immune system, including activation and activity of neutrophils, macrophages, T lymphocytes, and B lymphocytes. With burns of more than 20% TBSA, impairment of these immune functions is proportional to burn size.

Macrophage production after burn is diminished, which is related to the spontaneous elaboration of negative regulators of myeloid growth. This effect is enhanced by the presence of endotoxin and can be partially reversed with granulocyte colony-stimulating factor (G-CSF) treatment or inhibition of prostaglandin E_2. Investigators have shown that G-CSF levels actually increase after severe burn. However, bone marrow G-CSF receptor expression is decreased, which may in part account for the immunodeficiency seen in burns. Total neutrophil counts are initially increased after burn, a phenomenon that is related to a decrease in cell death by apoptosis. However, neutrophils that are present are dysfunctional in terms of diapedesis, chemotaxis, and phagocytosis. These effects are explained, in part, by a deficiency in CD11b/CD18 expression after inflammatory stimuli, decreased respiratory burst activity associated with a deficiency in p47-phox activity, and impaired actin mechanics related to neutrophil motile responses. After 48–72 h, neutrophil counts decrease somewhat like macrophages with similar causes.

T-helper cell function is depressed after a severe burn that is associated with polarization from the interleukin-2 and interferon-γ cytokine-based T-helper 1 (Th1) response toward the Th2 response. The Th2 response is characterized by the production of interleukin-4 and interleukin-10. The Th1 response is important in cell-mediated immune defense, whereas the Th2 response is important in antibody responses to

infection. As this polarization increases, so does the mortality rate. Burn also impairs cytotoxic T-lymphocyte activity as a function of burn size, thus increasing the risk of infection, particularly from fungi and viruses. Early burn wound excision improves cytotoxic T-cell activity.

4 Summary and Conclusion

Burn causes a distinct and complex responses that are delineated by time effects that are substantially change over time (Fig. 5). Thermal injury results in massive fluid shifts from the circulating plasma into the interstitial fluid space causing hypovolemia and swelling of the burned skin. When burn injury exceeds 20–30% TBSA, there is minimal edema generation in non-injured tissues and organs. The Starling forces change to favor fluid extravasation from blood to tissue. Rapid edema formation is predominating from the development of strongly negative interstitial fluid pressure (imbibition pressure) and to a lesser degree by an increase in microvascular pressure and permeability. Secondary to the thermal insult there is release of inflammatory mediators and stress hormones. Circulating mediators deleteriously increase microvascular permeability and alter cellular membrane function by which water and sodium enter cells. Circulating mediators also favor renal conservation of water and salt, impair cardiac contractility and cause vasoconstrictors, which further aggravates ischemia from combined hypovolemia and cardiac dysfunction. The end result of this complex chain of events is decreased intravascular volume, increased systemic vascular resistance, decreased cardiac output, end-organ ischemia, and metabolic acidosis. Early excision of the devitalized tissue appears to reduce the local and systemic effects of mediators released from burned tissue, thus reducing the progressive pathophysiologic derangements. Without early and full resuscitation therapy, these derangements can result in acute renal failure, vascular ischemia, cardiovascular collapse, and death. Edema in both the burn wound and particularly in the non-injured soft tissue is increased by resuscitation. Edema is a serious complication, which likely contributes to decreased tissue oxygen diffusion and further ischemic insult to already damaged cells with compromised blood flow increasing the risk of infection. Research should continue to focus on methods to ameliorate the severe edema and vasoconstriction that exacerbate tissue ischemia. The success of this research will require identification of key circulatory factors that alter capillary permeability, cause vasoconstriction, depolarize cellular membranes, and depress myocardial function. Hopefully, methods to prevent the release and to block the activity of specific mediators can be further developed in order to reduce the morbidity and mortality rates of burn shock. The profound and overall metabolic alterations post-burn associated with persistent changes in glucose metabolism and impaired

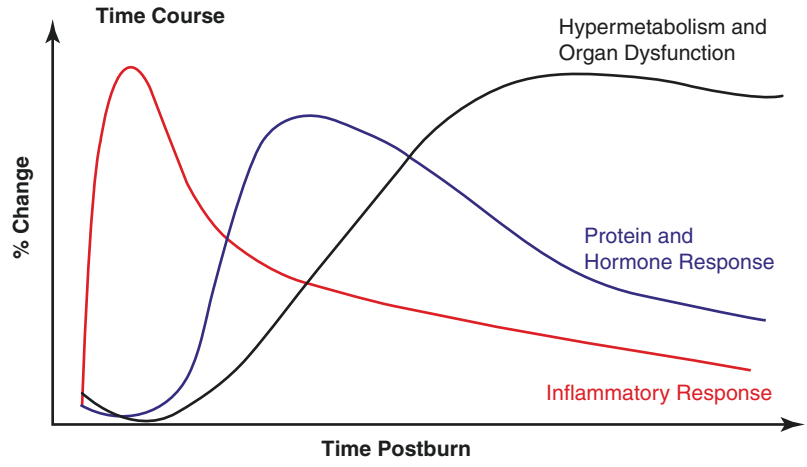

Fig. 5 Time course pattern of inflammatory response (red), protein and acute phase response (blue), and hypermetabolism and organ dysfunction (black). It is striking how long hypermetabolism and therefore catabolism and organ dysfunction persist

insulin sensitivity also significantly contribute to adverse outcome of this patient population and constitute another challenge for future therapeutic approaches of this unique patient population.

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Acute Burn Surgery

Alexandru-Cristian Tuca, Raimund Winter, and Lars-Peter Kamolz

1 Introduction

Burn care has markedly improved over the last decades. The probability to survive extent burn injuries is higher than ever before (Fig. 1). Thus, the main goal of current burn care extends beyond the preservation of life to re-integration of burn victims into their families, communities, work, and daily life. But before this can be achieved, the patient has to survive. Beside intensive care treatment, evaluation of sepsis using the current sepsis-3 definition/criteria, adequate analgesia, enough resuscitation, and prevention of infections the surgical intervention is a central aspect of the whole treatment in acute burns. This chapter describes the surgical part on how to handle acute burn injuries.

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2 Burn Wound Evaluation

One of the major challenges any burn surgeon must face is the decision on the nature of the further treatment of his or her burn patient (i.e., conservative versus surgical treatment). This decision depends on factors like localization, depth, and extent of the burn injury. However, current literature agrees that accurate burn wound evaluation is crucial for the further treatment. Today, there are many tools which can assist when it comes to the evaluation of burn depth and burn extent. Just to mention the Laser Speckle and Laser Doppler for burn depth assessment or different software tools like Burn Case 3D or the Rapid Burn Assessor mobile app for objective burn size evaluation.

3 Escharotomy/Fasciotomy

In burn surgery, the indication for an immediate surgical intervention occurs in the presence of circumferential deep burns affecting the upper/lower extremities or the chest wall. While in the extremities the development of a compartment syndrome is the main problem, in the chest wall ventilation problems can occur due to chest wall restriction. In order to prevent compartment syndrome or ventilation problems, an escharotomy should be performed. In high-voltage burn injuries, a fasciotomy of the different muscle compartments of the upper/lower extremity should be considered too.

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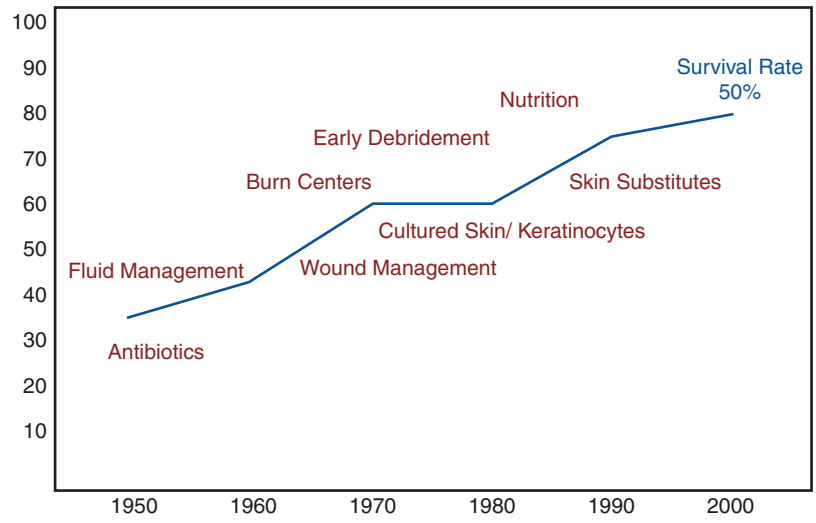

Fig. 1 Factors which had major impact on survival. The 50% survival rate has increased from 35% TBSA to 80% TBSA within the past decades

4 Surgical Burn Wound Management

Once the decision has been taken whether an escharotomy/fasciotomy is necessary, the next steps for the surgical treatment must be planned. The main goal of the surgical treatment is the replacement of the destroyed necrotic tissue. Superficial dermal burns will heal without operation within 2–3 weeks, but deep dermal and full-thickness burn will require operation. It is widely accepted that if skin does not regenerate within 3 weeks, morbidity and scarring will be severe. Further, it has become apparent that early excision is better than late excision because after 7 days the incidence of sepsis and graft failure increases. So, the trend regarding the treatment of deep dermal and full-thickness burns is going towards very early excision and grafting within 72 h after injury in order to reduce the risk of infection, decrease scar formation, shorten hospital stay, and thereby reduce total costs.

The excision of the necrotic tissue should be performed whenever the patient is hemodynamically stable. The operation should never be carried out if the patient is unstable and the risk of mortality is increased. In that case, the operation should be suspended until the patient is sufficiently stable. In patients associated with additional risk factors such as inhalation injury, patients of high age, or patients with cardiac problems, the surgical treatment differs and the decision when and how much to excise should be evaluated individually from case to case.

Sequential layered tangential excision to viable bleeding points, even to fat, while minimizing the loss of viable tissue, is the generally accepted technique. Excision of burn wounds to the fascia is reserved for large and deep burns where the risks of massive blood loss and the possibility of skin slough from less vascularized grafts on fat may lead to higher mortality. Enzymatic debridement with bromelain-based agents (e.g., Nexobrid®) is an alternative method to debride smaller deep dermal and non-life-threatening burns. The advantage is that it selectively removes the eschar without damaging the vital dermis.

After tangential excision of deep dermal burn injuries, the resulting defects can be covered with autologous or allogeneic skin grafts, xenografts, keratinocytes, or by use of synthetic materials like Suprathel ® (Fig. 2). In case of full-thickness burns, we dominantly use autografts to cover the wounds if there are enough available donor sites. In large burns, we normally use expanded autografts (mesh or Meek). Expansion rates of graft to wound area cover ranges from 1:1 to 1:9.

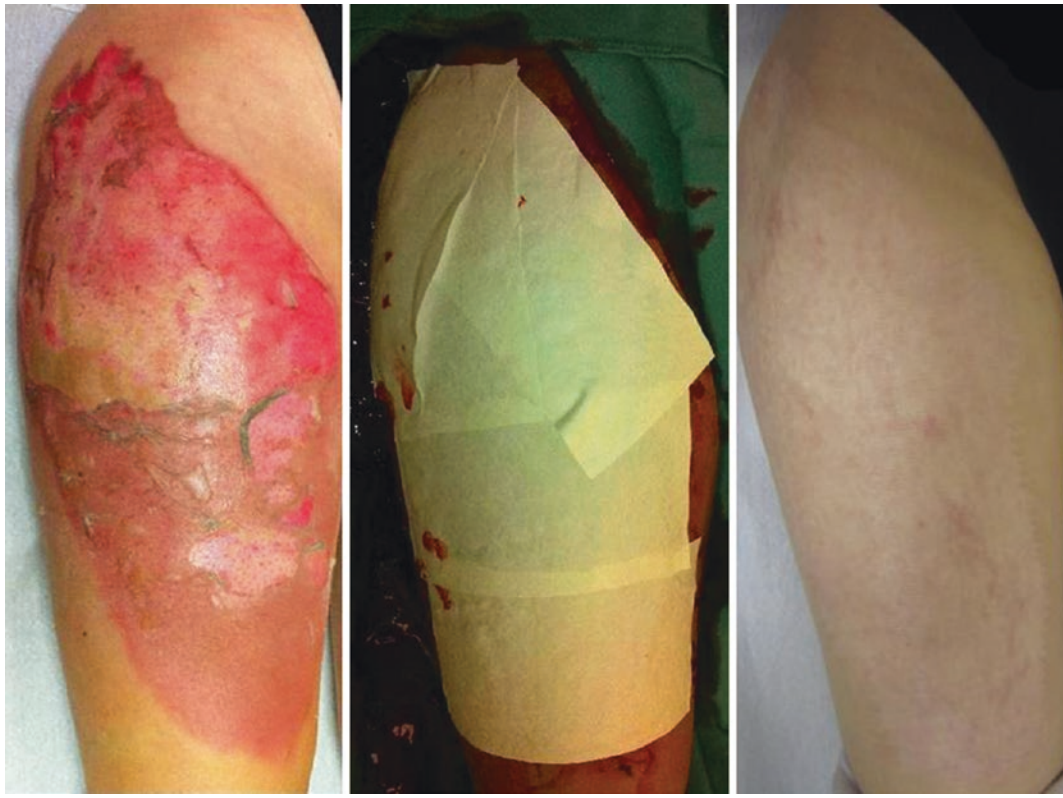

Fig. 2 Superficial to deep dermal burn—tangential excision of the deeper parts and coverage with Suprathel®, late results

Expansion rates higher than 1:3 heal in a suboptimal manner leading to contractures and unstable scars. Therefore, we like to combine these large meshed autografts in combination with allografts (Fig. 3) or keratinocytes (sandwich technique), or we will use the Meek technique (Fig. 4). In functional important regions like hands and over joints, a combined reconstruction of skin by use of a dermal matrix (Integra®, Matriderm®) and split-thickness skin graft seems to be superior to skin grafts alone (Fig. 5).

Donor sites for autografts in smaller burns, less than 40% total body surface area are seldom a problem unless the patient has a higher risk for surgical complication resulting from age, cardiopulmonary status, or coagulopathy. In patients with very extensive burns >60 total body surface area, the scarcity of harvesting areas for autologous skin grafts is one of the main problems. Therefore, we use cadaver skin (allografts) or xenografts (Fig. 6) as a temporary transplant and cover. These temporary transplants decrease the size of open wound until autografts become available as the partial-thickness burn area is healed or previously harvested donor sites heal.

This temporary covering helps to:

- Control wound infection.
- Prevent wound contracture.
- Relieve pain.

Sometimes, since burn wounds are often a mosaic of different burn depths, different techniques are combined in order to optimize burn wound closure regarding healing time and skin quality (Fig. 7).

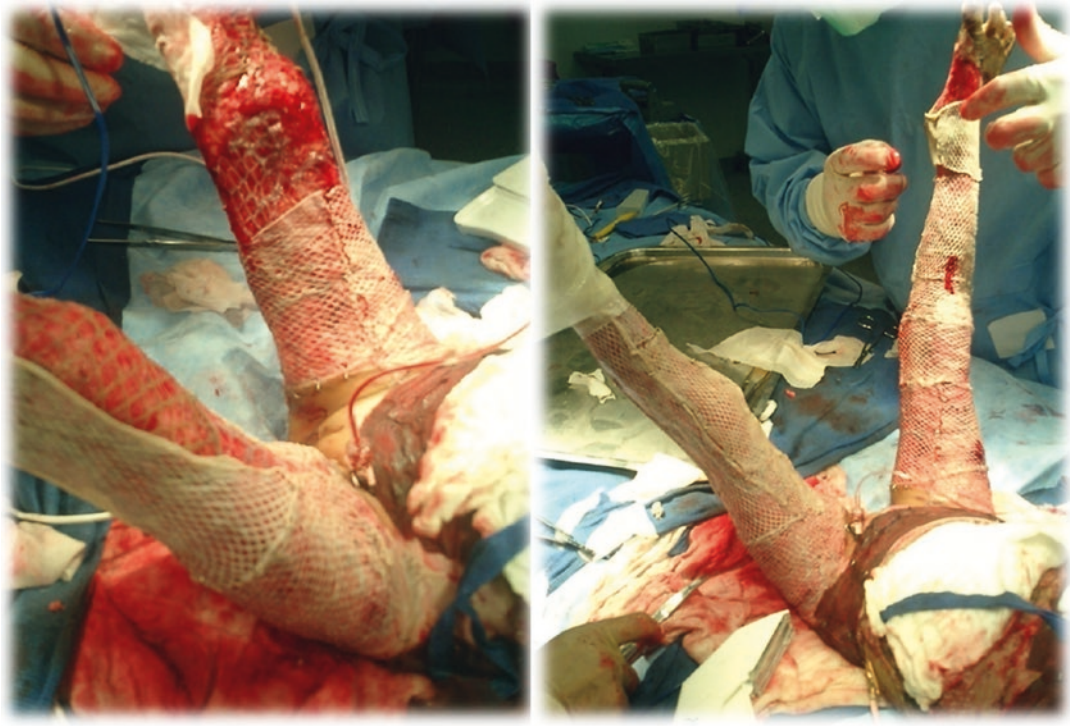

Fig. 3 "Sandwich technique": widely expanded autografts in combination with less expanded allografts

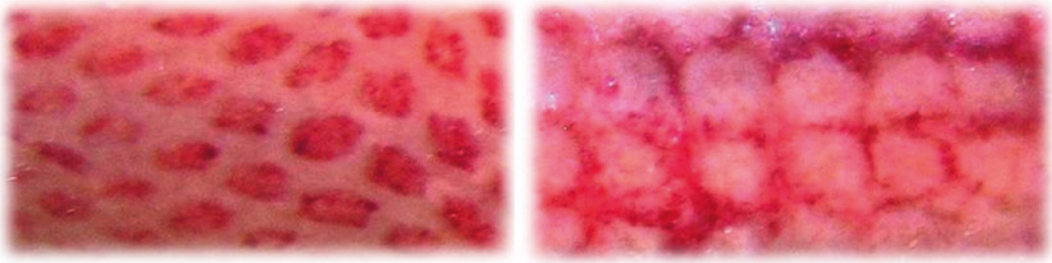

Fig. 4 Direct comparison of mesh and Meek grafted area

5 Location-Specific Treatment

5.1 Face

Deep dermal burns will be debrided and covered with keratinocytes or by silver-containing dressings like Acticoat Flex®. Full-thickness burns will be excised and grafted with unmeshed skin grafts according to aesthetic units of the face.

5.2 Hands

Deep dermal burns will be debrided and covered with keratinocytes, unmeshed skin grafts, or synthetic materials like Suprathel®. Full-thickness burns will be excised and grafted with unmeshed skin grafts, sometimes in combination with dermal substitutes.

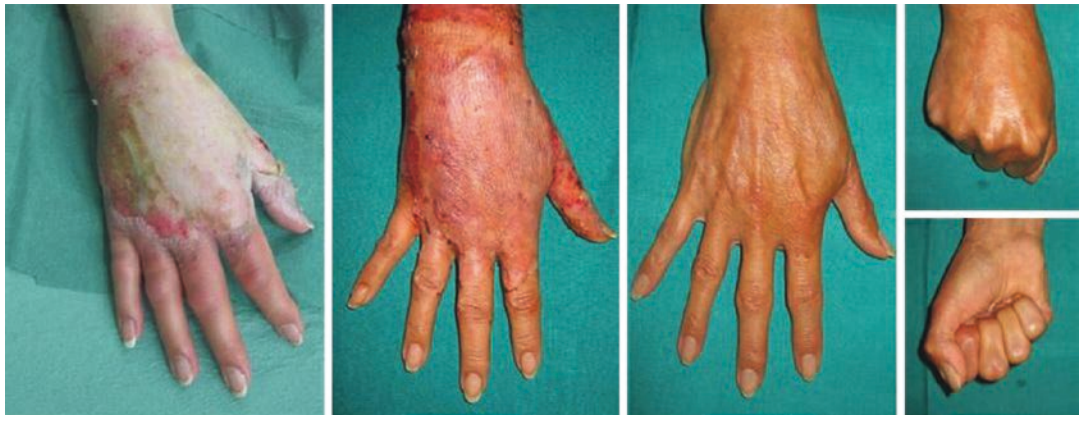

Fig. 5 Dermal to full thickness burn: excision and combined grafting (Matriderm® and unmeshed skin graft); early and late results

Fig. 6 Pig Skin (EZ-Derm®) as a temporary coverage of full-thickness burns in case of a lack of donor sites for autologous skin grafting

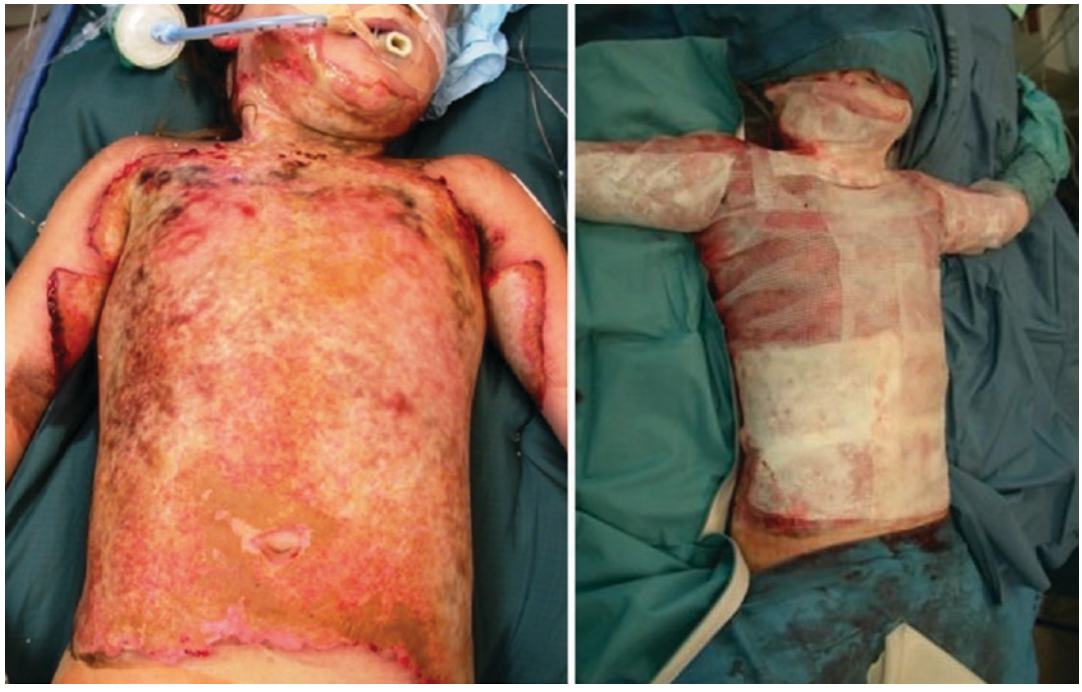

Fig. 7 Dermal to full-thickness burn: tangential excision and grafting: deep dermal parts with Suprathel®, full-thickness parts with meshed skin grafts (1:2)

6 Treatment Standards in Burns Larger than Sixty Percent Total Body Surface Area

Body regions can be organized according to the probability of skin take rate, functional importance, and ultimately determined for surgical priority (Figs. 8 and 9). The aim of the surgical approach is to remove the necrotic tissue within 9 days after injury; in large burns, the dorsal aspects of the lower extremities, dorsum, gluteal and dorsal femoral regions can be preferably preconditioned in a fluidized microsphere beads-bed, and the final debridement is normally not performed before days 10–14 after injury. Excision and grafting sessions can be organized in a timeline scheme described in Fig. 9:

Definition	Body region
funtional & aesthetic importance	face hands feet
superior take-rate	thorax, abdomen upper limb lower limb
inferior take-rate	flanks of torso gluteal region dorsal aspect of thighs

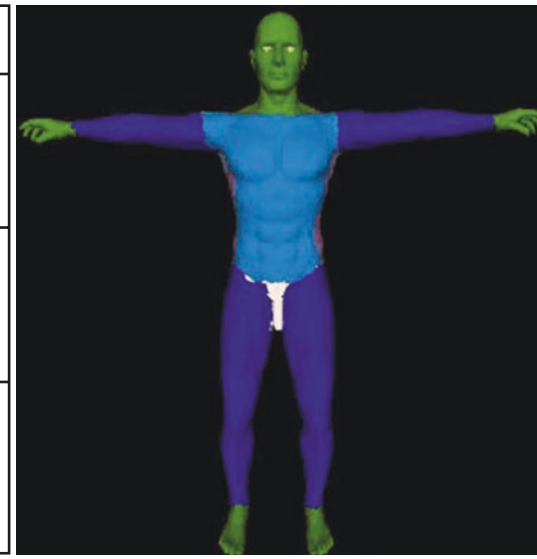

Fig. 8 Body region organization based on the functional importance and take rate

Fig. 9 Surgical timeline (This is an example for a typical surgical timeline; there might be differences in different countries and from center to center)

Timeline	Body region	Preferred technique
Day 3-9	hands	unmeshed split-thickness skin grafts (STSG)
	thorax, abdomen upper extremity ventral lower extremity	Meek (1:6 or 1:9) Mesh (1:1.5 or 1:3)
Day 10-14	face	unmeshed (STSG)
	dorsum dorsal lower extremity gluteal regions dorsal aspect of thigh	Meek (1:6 or 1:9) Mesh (1:1.5 or 1:3)
> Day 14	residual defects	Mesh (1:1.5 or 1:3)

- In young and clinically stable adult burn patients, we aimed to remove necrotic tissue and provide cover for full-thickness burns in two operative sessions within the first 14 days after injury.
- Individuals aged 65 years and above usually required more than two operative sessions within the first 14 days because the area operated on per session had to be restrained and adapted to the patient' general condition.

Whenever possible, unmeshed split-thickness skin grafts (STSG) are used for face and hands; all other areas are covered with either Meek grafts (expansion ratio 1:6 or 1:9) or, if respective donor sites enough, with mesh grafts using an expansion ratio of 1:1.5 or 1:3. Expansion ratios exceeding 1:3 to achieve sufficient coverage for full-thickness burns are regarded as indication for using the Meek technique (1:6 or 1:9).

7 Temporary Coverage

If harvested STSG did not suffice for coverage of full-thickness areas (i.e., third degree), we prefer to use allogeneic STSG as a temporary alternative. However, if allogeneic skin is not available, we use xenografts or a synthetic material (e.g., Epigard®) to temporarily cover debrided full-thickness areas.

Further, allograft is also used for protection of widely meshed autografts (>3:1 mesh) during healing. The allograft is applied over the meshed autograft in sandwich technique (Fig. 3). Surgical priority is given to areas of functional and aesthetic importance and superior take rate. Body regions with inferior take rate are normally preconditioned.

8 Fluidized Microsphere Beads-Bed

Fluidized microsphere beads-beds are good method for wound preconditioning but also for postoperative wound care. It removes moisture in order to keep the burn wounds dry and to permit maintenance of constant temperature levels in areas in direct contact with the bed's superficial fabric. Only thin sterile covers are employed to shield dorsal burned areas while in these beds, and no extra ointments are applied. For wound coverage of freshly operated areas, we prefer to use fatty gauzes and dry sterile compresses. Patients with arising difficulties in respiratory management or temperature control while in fluidized microsphere beads-beds are temporarily transferred to standard intensive care beds.

9 Negative-Pressure Wound Therapy (Vacuum-Assisted Closure)

Negative-pressure wound therapy or vacuum-assisted closure (VAC®) can be used in the local therapy of STSG receiver regions of inferior take and allowed for early mobilization in functionally important zones.

9.1 Early Mobilization

Early individual physiotherapy and ergotherapeutic splinting accomplishes the therapeutic strategy.

10 Nutrition and Anabolic Agents

Catabolism as a response to thermal trauma can only be modulated, not completely reversed. The burn wound consumes large quantities of energy during the healing process due to the large population of inflammatory cells and the production of collagen and matrix by fibroblasts. Therefore, adequate nutrition is of utmost importance for burn wound healing.

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Critical Care of Burn Victims Including Inhalation Injury

Marc G. Jeschke

1 Introduction

There is no greater trauma than major burn injury which can be classified according to different burn causes and different depths. More than 500,000 burn injuries occur annually in the United States per year [1]. Although most of these burn injuries are minor, approximately 40,000 to 60,000 burn patients require admission to a hospital or major burn center for appropriate treatment. The devastating consequences of burns have been recognized by the medical community and significant amounts of resources and research have been dedicated, successfully improving these dismal statistics [2–4]. Specialized burn centers and advances in therapy strategies, based on improved understanding of resuscitation, protocolized and specialized critical care, enhanced wound coverage, more appropriate infection control, improved the treatment of inhalation injury and better support of the hypermetabolic response to injury have further improved the clinical outcome of this unique patient population over the past years [4, 5]. However, severe burns remain a devastating injury affecting nearly every organ system and leading to significant morbidity and mortality [2–6]. Of all cases, nearly 4000 people die of complications related to thermal injury [2].

Burn deaths generally occur either immediately after the injury or weeks later as a result of infection/sepsis, multisystem organ failure, or hypermetabolic catabolic responses [5, 7]. Therefore, this chapter is divided into critical care during the early phases and later phases. The quality of the complex care of burn patients is directly related to the outcome and survival of burn patients. The key aspects for the care are:

1. **Initial care at the scene and pre-hospital**: adequate and timely response, evaluation of the burns, treatment of the burn patient, resuscitation, initial pain and transport.
2. **Early hospital phase**: admission to a burn center, escharotomies/fasciotomies, resuscitation, treatment of inhalation injury, critical care to maintain organ perfusion and function.
3. **Later hospital phase**: wound care including burn surgeries, infection control, attenuation of hypermetabolism, and maintaining organ function.

In this chapter, we focus on critical care components that have been shown to contribute to increased post-burn morbidity and mortality and are typical hallmarks of critical care responses.

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As Chap. 1 delineated pre-hospital, fluid, and early management, we will focus on early hospital phase and later hospital phase.

2 Initial and Early Hospital Phase

The initial management and therapeutic goal for these patients is prevention of organ failure, which begins with adequate resuscitation [8–12]. Resuscitation and all current formulas are discussed in detail in Chap. 1. Resuscitation is however also one of the key aspects of the early phase in critical care. Once the burn patient is received by the accepting burn center the patient usually is evaluated and treated in the tub room. This visit includes cleansing, evaluation of burn wounds, possible escharotomies/fasciotomies, intubation incl. Bronchoscopy and diagnosis of inhalation injury, placement of arterial and venous access, Foley catheter, and adequate dressing care. Once these interventions are finished the central element of critical care is monitoring of vital signs:

- Invasive arterial blood pressure.
- Noninvasive blood pressure (not recommended for large burns >40% TBSA).
- Urine output.
- CVP.
- Oxygen saturation.
- Respiratory rate.
- Blood gas with lactate.
- Ventilation settings.
- Invasive and noninvasive thermodilution catheter (e.g., PiCCO catheter to monitor CO, CI, SVR, SVRI, ETBV, lung water).
- Serum organ marker (liver, kidney, pancreas, endocrine system).
- Central and peripheral tissue perfusion.

2.1 Blood Pressure

Continuous monitoring of the arterial blood pressure ensures adequate organ perfusion and is a key aspect in the initial post-burn phase. In general, an MAP of >60–65 mmHg should be maintained. Chronic hypertensive patients may require a greater MAP which can vary. The most common problem during the first 24–48 h post-burn is hypotension with very few patients having hypertension. Adequate MAP and organ perfusion can be achieved by:

- Adequate fluid resuscitation (e.g., Parkland 4 cc/kg/m^2 burn of RL).
- Albumin substitution after 8–12 h post-burn if resuscitation fails (5% albumin 75–125 cc/h).
- Transfusion of PRBC.
- Dobutamin if cardiac index low (5–10 yg/kg/min).
- Vasopressin if patient experiences vasodilation and low MAP (1.2–2.4 IU).
- Norepinephrine or epinephrine persistent and refractory hypotension.

If a patient is hypertensive (systolic > 200 mmHg or diastolic > 120 mmHg) and has signs of over-resuscitation decrease vasopressors, decrease fluids, and decrease albumin in stages until MAP is targeted. If the patient is on no vasopressors, inotropes, and hypertensive, recommendations are

- Nitroprusside (>0.5 yg/kg/min).
- Labetalol (10–20 mg).
- Nicardipine (5 mg/h).
- Nifedipine (5 mg sublingual).

2.1.1 Resuscitation

Adequate resuscitation is a key element of early urn critical care [8–12]. Maintenance of organ perfusion during burn shock depends upon restoration of intravascular volume. The most common algorithm, the Parkland formula, calculates a total volume of crystalloid to be given over the first 24 h according to: 4 cc/kg (patient weight)/%TBSA (Total Body Surface Area burnt) [8, 13–15]. In accordance to the American Burn Association (ABA), the resuscitation formula is only to be used as a guideline for resuscitation in burn shock [9–11, 14, 16]. The Parkland is deficient in calculating the fluid requirements for resuscitation in patients with: large burn size/deeper burns; inhalation injury; delays in resuscitation; alcohol or drug use;

as well as those with electrical injury leading to inadequate/inappropriate resuscitation. The endpoints (urine output of 0.5 cc/kg/h, MAP > 65), which traditionally had been used for fluid resuscitation, are not always adequate. With the advent of goal-directed therapy [8, 13–15, 17], it has become apparent that the Parkland formula can underestimate or overestimate fluid requirements. However, with this discovery and efforts to improve fluid resuscitation, patients with severe burns receive far greater crystalloid volumes than predicted by the Parkland formula resulting in "fluid creep" [9, 10, 15, 18] with its inherent complications such as pulmonary edema, pleural effusions, pericardial effusions, abdominal compartment syndrome, extremity compartment syndrome, and conversion of burns to deeper wounds. In addition, increasing fluid requirements in burn patients significantly increased the risk of developing ARDS, pneumonia, bloodstream infections, multi-organ failure, and death [16]. Given the risk of abdominal compartment syndrome with large burn and its dire consequences, intra-abdominal pressure monitoring is therefore recommended in the burns involving more than 30% TBSA [19].

A recent initiative by the ABA is to resuscitate a patient with 2 cc/kg/%TBSA. This volume moved forward in order to reduce fluid creep. Its efficacy and adequacy remains to be determined.

Another new initiative for adequate resuscitation is the Computerized Decision Support (CDS). Recently, a predictive model and infusion algorithm was developed for adult patients to guide hourly fluid rates. The Salinas model was based on data from 39 burn patients that related fluid infusions to burn size and resultant UO [20]. One commercialized computerized decision support tool (Arcos Burn Navigator) incorporates the Salinas model to provide hourly decision support along with novel resuscitation displays that provide situational awareness of the fluid status and UO levels during the resuscitation process [21]. One display is a volume graph showing total infused fluids infused since time of burn, with Baxter and Modified Brooke guidelines overlaid and total 24 h volume projection (Fig. 1). A single-center

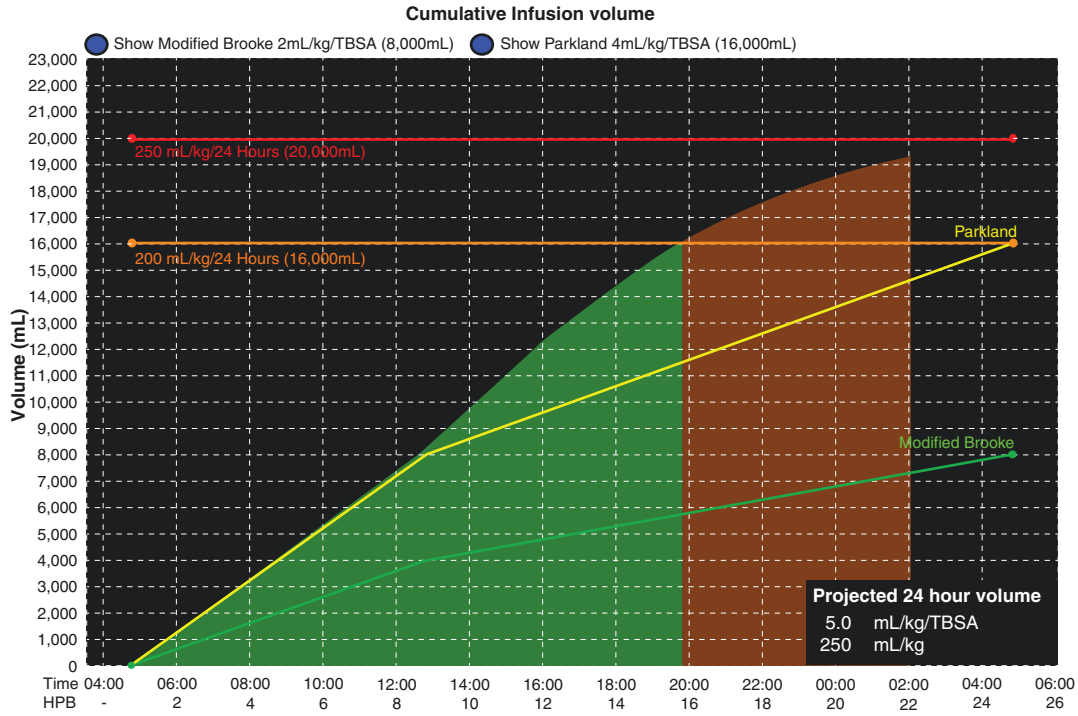

Fig. 1 A volume graph showing current volume (green/orange), Parkland (yellow) and Modified Brooke (bright green) guidelines, and projected 24 hour fluid volume

cohort study showed that computerized decision support can increase how often patients meet UO goals, reduce total fluids given, reduce ventilator days, and may contribute to a reduction in mortality [20]. Current CDS approaches face two main limitations: manual data entry and fluid "non-responders," who are generally defined as patients whose urine output does not increase after increasing infusion rates or patients whose UO is adequate but only with excessively high infusion rates and a large positive net fluid balance. Patients with a total infused volume over 250 mL/kg, regardless of burn size, are at risk for abdominal compartment syndrome, which is associated with high rates of morbidity and increased mortality.

In general, the initial resuscitation should aim to maintain organ perfusion: urinary output 0.5 ml/h, lack of tachycardia, maintenance of MAP ≥60 mmHg, normal lactate, and base excess levels will generally reflect this global condition [2, 15, 16]. As mentioned before the majority of burn surgeons will use the Parkland formula for the first 24 h. It is imperative to look for signs of adequate, over-, and under-resuscitation (Table 1).

After 24–48 h, the patients generally become spontaneously hyperdynamic and the fluid delivery should be drastically reduced to about 30–40% of that infused during the first 24 h. The total daily maintenance in terms of fluid requirements can be calculated by:

$$\text{Basal fluid } 1500\,\text{cc/m}^2 + \text{evaporative water loss}\left[\left(25 + \%\text{burn}\right) * \text{m}^2 * 24\right] = \text{total maintenance fluid; m}^2 \text{ in meter square}$$

However, calculated fluid balances are difficult to calculate, as they do not take into account the exact amount of exudative losses through the burn wounds (about 0.5–1 l/10% TBSA/day). The condition may be complicated by the used of fluidized or air beds, which cause an even greater loss of free water. By day 3, the interstitial fluids that have accumulated during the first 24–48 h must be mobilized and excreted. This generally required an active stimulation of diuresis using loop diuretics (generally Furosemide) and sometimes in combination with an aldosterone antagonist Aldactone.

Table 1 criteria for assessment of under and over-resuscitation

Under-resuscitation	Over-resuscitation
Oliguria <0.3 ml/kg/h	Polyuria >1.0 ml/kg/h
Hemoglobin >180 g/l (Ht > 55%)	Decreasing PaO_2/FiO_2 → pulmonary edema
Natremia >145 mmol/l	Increasing PAPO / PVC
Cardiac index <2 l/min/m^2	Rapidly increasing cutaneous edema
SvO_2 < 55%	Fluid delivery > Ivy index (fluid delivery > 250 ml/kg BW)
Plasma lactate >2 mmol/l or increasing	Intra-abdominal P > 20 mmHg → intra-abdominal hypertension leading to → acute renal failure, splanchnic ischemia, transformation of 2°–3° burns, compartment syndrome in limbs (↑need for fasciotomies), ↓venous return with hemodynamic failure
Base excess < −5 mmol/l or decreasing	

2.1.2 Albumin

The use of albumin in burn patients is not well defined and to date no prospective randomized trial in burn patients shows the advantage or disadvantage of albumin administration for burn resuscitation, maintenance, or burn infection/sepsis [10, 22]. A lot of burn care providers believe that albumin has a positive effect in the case of burn resuscitation as a rescue modality. In general, in case of hypoalbuminemia <20 g/l the colloid osmotic pressure shifts to the extent that fluid is not resorbed and therefore fluid stays in the interstitial space enhancing edema formation. We believe that albumin should be used for difficult resuscitations and we believe that hypoalbuminemia <20 g/l should be corrected to avoid the negative consequences of decreased oncotic pressure.

2.1.3 Transfusion

Transfusion guidelines are currently being investigated and most like changed. The gold standard of 100 mg/dl has been questioned and a large multicenter trial is ongoing and investigates transfusions thresholds 70 mg/dl vs. 100 mg/dl.

Our practice is to target a level of least 70 mg/dl, but if a patient is premorbid with impaired cardiac function or poor oxygen delivery we consider reaching hemoglobin levels of 80 mg/dl.

2.1.4 Vasopressors

Vasopressors or inotropes can be used if indicated. Usually, during the first 8–12 h vasopressors should be avoided as vasoconstriction can have adverse effects. However, Dobutamine as an inotrope can improve cardiac function if CO or CI is low (<3). Classical vasopressors epinephrine and norepinephrine should be used with caution. Vasopressin is becoming a possibility that is currently studied in various trials. In the critical care population, vasopressin did not improve outcome compared to catecholamines. In addition, there are case reports that no benefit with vasopressin but an increased incidence of adverse effects, which is usually associated with high doses of vasopressin (>2.4 IU). However, it appears that doses between 1.2 and 2.4 IU are relatively safe and can improve the blood pressure. Our center usually uses vasopressin as a second-line agent. Dopamine another inotropic agent is used by some but generally is not widely used for burns.

2.2 Urine Output

Urinary output in the acute phase of a burn is indicative of adequate organ perfusion and the suggested target is 0.5–1 cc/kg/h. In children, UOP is targeted to 1 cc/kg/h. However, UOP is not always adequate and can be affected by the burn itself, infusion of antioxidants during resuscitation, central or peripheral renal insufficiency.

2.3 CVP

CVP is a rough marker for preload and hence filling of the patient. Of importance is that CVP should be measured correctly at the level of the heart with a subclavian or jugular line in place. The range of an adequate CVP in burned adults 4–8 mmHg, which is 2–6 in burned children.

2.4 Respiration

Respiratory rate, respiratory effort, breath sounds, and skin color reflect oxygenation and provide objective measurements of breathing. A respiratory rate of less than 10 or greater than 60 is a sign of impending respiratory failure. Use of accessory muscles, manifested by supraclavicular, intercostal, subcostal, or sternal retractions, as well as the presence of grunting or nasal flaring, are signs of increased work of breathing. Auscultation of breath sounds provides a clinical determination of tidal volume. Skin color deteriorates from pink, to pale, to mottled, to blue as hypoxemia progresses. These signs must be followed throughout the primary survey to avoid respiratory failure. Patients with probable respiratory failure should receive rapid, aggressive, and definitive airway management.

Oral intubation with the largest appropriate endotracheal tube is the preferred method for obtaining airway access and should be accomplished early if impending respiratory failure or ventilatory obstruction is anticipated.

Oxygen saturation in the initial phase but also during the later phase of hospitalization should be over 85–90. Respiratory should be 8–20 in adults and 14–38 in children.

Effective gas exchange should be determined in an arterial blood gas analysis. Targets for good oxygenation as well as organ perfusion are: pH >7.25.

2.4.1 Ventilation Settings

The different modes of ventilation including high frequency oscillation are all being investigated and tested. Detailed descriptions of the different modes are beyond the scope of this handbook. In short, PEEP is useful in supporting oxygenation. The level of PEEP required should be established by empirical trials and reevaluated on a regular basis. PEEP levels should start at 5 cmH_2O and be increased in 2–3 cm increments. PEEP trials should be done to optimize oxygenation and cardiac output. The effectiveness of continuous positive airway pressure (CPAP) or PEEP is related to surface tension abnormalities and the marked tendency for atelectasis in these patients.

Pressure control ventilation with permissive hypercapnia is the current preferred method of treatment for ventilated patients. If pulmonary edema continues, the amount of PEEP and of oxygen should be elevated so as to maintain adequate gas exchange. The use of high frequency oscillating ventilators in the pressure control mode may also result in better removal of airway debrid. Low tidal volumes (5–8 ml/kg) with PEEP may be needed to improve oxygenation. Peak flow rates should be adjusted as needed to satisfy patient inspiratory demands. Inspiratory/Expiratory (I:E) ratio: the inspiratory time should be long enough to deliver the tidal volume at flow rates that will not result in airway turbulence and high peak airway pressures. The normal I:E ratio 1:2. This may be adjusted to increase the ratio if oxygenation becomes difficult. Inspired oxygen concentration as a starting point and until the level of hypoxemia is determined, a patient placed on a ventilator should receive an oxygen concentration of 100%. Decrease the FiO_2 as ABGs improve.

Ventilator management: (guideline from the American College of Chest physicians) targeted should be an acceptable oxygen saturation a plateau pressure of greater than 35 cmH_2O is cause for concern (clinical conditions that are associated with a decreased chest wall compliance, plateau pressures greater than 35 cmH_2O may be acceptable). To accomplish the goal of limiting plateau pressures, PCO_2s should be permitted to rise (permissive hypercapnia) unless other contraindications exist that demand a more normal PCO_2 or pH.

Extubation criteria

- In general early as possible!
- Criteria value.
- PaO_2/FiO_2 (P/F) ratio > 250.
- Maximum inspiratory pressure (MIP) (cmH_2O) > 60.
- Spontaneous tidal volume (ml/kg) > 5–7.
- Spontaneous vital capacity (ml/kg) > 15–20.
- Maximum voluntary ventilation > twice the minute volume.
- Audible leak around the ET tube with cuff deflated.

2.5 Inhalation Injury

20–30% of all major burns are associated with a concomitant inhalation injury, with a mortality of 25 to 50% when patients required ventilatory support for more than 1 week post injury [2, 4, 23]. A significant portion of fire-related deaths result not from burn injury but from inhalation of the toxic products of combustion [14, 23–25]. Many of these compounds may act together, so as to increase mortality. This is especially true of carbon monoxide (CO) and hydrogen cyanide (HCN) where a synergism has been found to increase tissue hypoxia and acidosis and may also decrease cerebral oxygen consumption and metabolism. Cyanide (CN) toxicity associated with inhalation injury remains a diagnostic dilemma as markers for CN toxicity (elevated blood lactate, elevated base deficit, or metabolic acidosis) can also represent under-resuscitation, associated trauma, CO poisoning, or hypoxia. Regardless, aggressive resuscitation and administration of 100% oxygen remains a mainstay of treatment. Controversy remains as to the need for specific antidotes in cyanide poisoning [26]. The use of hydroxycobalamin (a standard of pre-hospital care in some Europe centers) has not been as widely accepted in North America. There is minimal evidence for the role of CN antidotes in smoke inhalation injury; therefore, aggressive supportive therapy aimed at allowing for the hepatic clearance of cyanide without specific antidotes should be the first line of treatment. Other possible contributing toxic substances are hydrogen chloride (produced by polyvinyl chloride degradation), nitrogen oxide, or aldehydes which can result in pulmonary edema, chemical pneumonitis, or respiratory irritability. Direct thermal damage to the lung is seldom seen except as a result of high pressure steam, which has 4.000 times the heat-carrying capacity of dry air. Laryngeal reflexes and the efficiency of heat dissipation in the upper airway prevent heat damage to the lung parenchyma.

The clinical course of patients with inhalation injury is divided into three stages:

- First stage: Acute pulmonary insufficiency. Patients with severe lung injuries show acute pulmonary insufficiency from 0 to 36 h after injury with asphyxia, carbon monoxide poisoning, bronchospasm, upper airway obstruction, and parenchymal damage.
- Second stage: Pulmonary edema. This second stage occurs in 5–30% of patients, usually from 6 to 72 h post-burn and is associated with a high mortality rate.
- Third stage: Bronchopneumonia appears in 15% to 60% of these patients and has a reported mortality of 50% to 86%. Bronchopneumonia occurs typically 3–10 days after burn injury is often associated with the expectoration of large mucus casts formed in the tracheobronchial tree. Those pneumonias appearing in the first few days are usually due to penicillin-resistant Staphylococcus species, whereas after 3–4 days, the changing flora of the burn wound is reflected in the appearance in the lung of Gram-negative species, especially Pseudomonas species.

Early detection of bronchopulmonary injury is critical in improving survival after a suspected inhalation injury. Clinical signs [14, 23, 27]:

- History of exposure to smoke in closed space (patients who are stuporous or unconscious).
- Physical findings of: facial burns/singed nasal vibrissae/bronchorrhea/sooty sputum/auscultatory findings (wheezing or rales).
- Laboratory findings: hypoxemia and/or elevated levels of carbon monoxide.
- Chest X-ray (insensitive method because admission studies are very seldom abnormal and may remain normal as long as 7 days post-burn).
- Bronchoscopy should be the standard diagnostic method on every burn patient. Inhalation injury can be graded using the scale of Gamelli et al. [25]:
  - No inhalation injury or Grade 0.
    Absence of carbonaceous deposits, erythema, edema, bronchorrhea, or obstruction.
  - Mild Injury or Grade I Injury.
    Minor or patchy areas of erythema, carbonaceous deposits in proximal or distal bronchi any or combination.
  - Moderate Injury or Grade II Injury.
    Moderate degree of erythema, carbonaceous deposits, bronchorrhea with or without compromise of the bronchi any or combination.
  - Severe Injury or Grade III Injury.
    Severe inflammation with friability, copious carbonaceous deposits, bronchorrhea, bronchial obstruction any or combination.
  - Massive Injury or Grade IV Injury.
    Evidence of mucosal sloughing, necrosis, endoluminal obliteration any or combination.
- To define parenchymal injury, the most specific method is the 133 Xe lung scanning, which involves intravenous injection of radioactive xenon gas followed by serial chest scintiphotograms. This technique identifies areas of air trapping from small airway partial or total obstruction by demonstrating areas of decreased alveolar gas washout.
- Additionally pulmonary function test can be performed and could show an increased resistance and decreased flow in those with abnormal 133 Xe scans.

The treatment of the inhalation injury should start immediately, with the administration of 100% oxygen via face mask or nasal cannula. This helps reverse the effects of CO poisoning and aids in its clearance, as 100% oxygen lowers its half-life time from 250 to less than 50 min. Maintenance of the airway is critical. If early evidence of upper airway edema is present, early intubation is required because the upper airway edema normally increases over 8–12 h. Prophylactic intubation without good indication however should not be performed. Intubation criteria see Table 2.

Several clinical studies have shown that pulmonary edema could not be prevented by fluid restriction. Indeed, fluid resuscitation appropriate for the patients other needs results in a decrease

Table 2 Indication for intubation [2, 4]

Criteria	Value
PaO_2 (mmHg)	<60
$PaCO_2$ (mmHg)	>50 (acutely)
P/F ratio	<200
Respiratory/ventilatory failure	Impending
Upper airway edema	Severe
Severe facial burn	
Burns over 40% TBSA	
Clinical signs of severe inhalation injury	

in lung water, has no adverse effect on pulmonary histology, and improves survival. Although overhydration could increase pulmonary edema, inadequate hydration increases the severity of pulmonary injury by sequestration of polymorphonuclear cells and leads to increased mortality.

Prophylactic antibiotics for inhalation injury are not indicated, but clearly are indicated for documented lung infections. Empiric choices for the treatment of pneumonias prior to culture results should include coverage of methicillin-resistant *Staphylococcus aureus* in the first few days post-burn (these develop within the first week after burn) and of Gram-negative organisms (especially Pseudomonas or Klebsiella) which mostly occur after 1 week post-burn. Systemic antibiotics regimes are based on serially monitored sputum cultures, bronchial washings, or transtracheal aspirates.

Pharmacological management:

- Bronchodilators (Albuterol) Q 2 h.
- Nebulized heparin 5.000 to 10.000 units with 3 cc normal saline Q 4 h which alternates with.
- Nebulized acetylcysteine 20%, 3 cc Q 4 h.
- Hypertonic saline induce effective coughing.
- Racemic epinephrine reduce mucosal edema.

The theoretical benefits of corticosteroid therapy include a reduction in mucosal edema, reduced bronchospasm, and the maintenance of surfactant function. However, in several animal and clinical studies mortality increased with the administration of corticosteroids and bronchopneumonia showed a more extensive abscess formation. Thus, the use of corticosteroids is contraindicated.

Prognosis: Inhalation injury is one of the most important predictors of morbidity and mortality in burn patients. When present, Inh-Inj increases mortality in up to 15 times [14, 23, 26, 28]. Inh-Inj requires endotracheal intubation, which in turn increases the incidence of pneumonia. As mentioned before, pneumonia is a common complication of Inh-Inj and increases mortality in up to 60% in these patients. Patients usually recover full pulmonary function and late complications are not the rule. Complications can be secondary to the Inh-Inj or to the endotracheal or tracheostomy tube. Hyperreactive airways and altered patterns on pulmonary function (obstructive and restrictive) have been described following Inh-Inj. Scarring of the airway can cause stenosis and changes in the voice, requiring voice therapy and occasionally surgery.

2.6 Invasive and Noninvasive Thermodilution Catheter (PiCCO Catheter)

A novel approach for burn patients has been the use of thermodilution catheters to determine cardiac function, resistance, and lung water [11, 29, 30]. The use of these catheters may enable focused and algorithm-driven therapy that may improve the resuscitation phase, but as of now there are only few small studies published that do not allow major conclusions. But these systems show promising results to optimize resuscitation [11].

Volume status and cardiac performance are especially difficult to evaluate in the burned victim. In particular, burned extremities may impede the ability to obtain a blood pressure reading by a sphygmomanometer (blood pressure cuff). In these situations arterial lines, particularly femoral lines are useful to monitor continuous blood pressure readings. Invasive hemodynamic monitoring via pulmonary artery

catheter (PAC) permits the direct and continuous measurement of central venous pressure (CVP), pulmonary capillary wedge pressure, cardiac output (CO), systemic vascular resistance (SVR), oxygen delivery (DO2), and oxygen consumption (VO2). PAC-guided therapy has been studied most extensively in trauma and critically ill surgical patients. It has been shown that hemodynamic data derived from the PAC appeared to be beneficial to ascertain cardiovascular performance in certain situations (inadequate noninvasive monitoring, difficulty to define endpoints of resuscitation). However, the general practicability, risk-benefit ratio, and lack of mortality reduction when using PAC have been widely criticized. At the moment, there are no studies in burn patients to provide evidence-based recommendations. In order to overcome the disadvantages of the PAC, less invasive techniques have been developed.

With transpulmonary thermodilution (TPTD), a cold saline bolus is injected into the central venous circulation, and the subsequent change in blood temperature is picked up by a thermistor-tipped arterial catheter. This is connected to a commercially available device (PiCCO®) that calculates flows and volumes from the dilution curves. In addition to CO and SVR measurement, TPTD allows an estimation of global end-diastolic volume (GEDV) and intrathoracic blood volume (ITBV), both indicators of cardiac preload, and extravascular lung water (EVLW), which is a marker of pulmonary edema. The use of TPTD goal-directed therapy based on ITBV and EVLW measurements in critically ill patients has been studied in various prospective trials and showed promising results, none of these however specific for burn patients.

In our center, we use an algorithm to optimize fluid resuscitation and cardiac performance in the acute setting as well as during the ICU stay [11] (Fig. 2):

2.7 Serum Organ Markers

In our opinion, it is imperative to follow organ function from the initial phase after injury throughout ICU and hospital stay. The most feasible approach is to measure serum markers of organ function or dysfunction/damage. We recommend [4].

- Cardiac markers: troponin, A- and B-natriuretic peptide, CK,
- Liver: AST. ALT, Bili, ALKP.
- Pancreas: Amylase, Lipase.
- Kidney: BUN, creatinine.
- Hematology: CBC including coagulation, Differential CBC including neutrohils and bands.
- Hormonal: Cortisol including ACTH challenge, thyroid axis, GnRH.

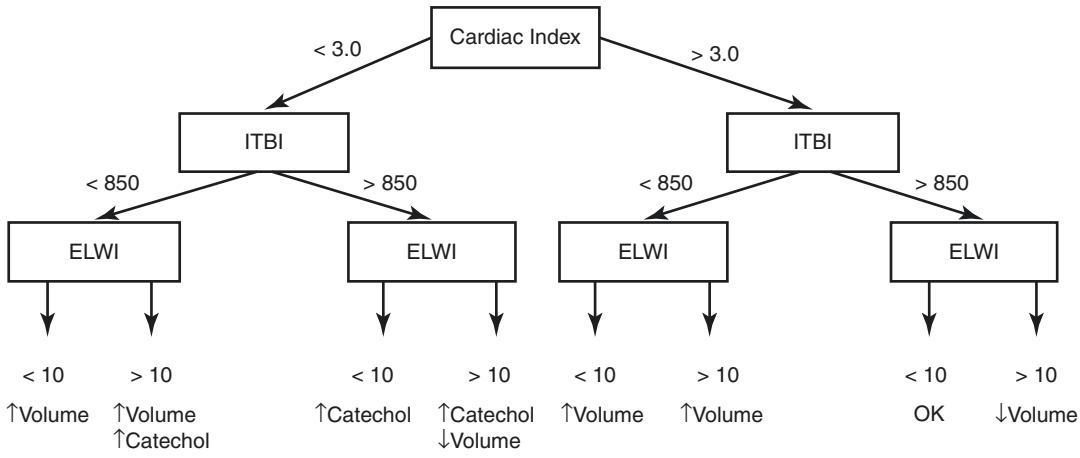

Fig. 2 Algorithm to treat resuscitation based on noninvasive monitoring

For longitudinal observation, it is recommended to obtain admission values and measures values once or twice per week.

3 Later Hospital Phase

The later phase includes critical practices to maintain organ function, control infection and sepsis, and alleviate hypermetabolism. This section will focus on maintaining organ function and complication of long-term ICU sequelae as infection and sepsis is discussed in detail in Chap. 5, and hypermetabolism is covered in Chap. 8.

3.1 Central Nervous System

Anoxic brain injury used to be the leading cause of death in burn patients, which has been replaced by sepsis and MOF [7]. Adequate resuscitation and early intubation improved mortality in burn patient [12, 14]. However, neurological disturbances are commonly observed in burned patients. The possibility of cerebral edema and raised intracranial pressure must be considered during the early fluid resuscitation phase, especially in the case of associated brain injury or high voltage electrical injury. Inhalation of neurotoxic chemicals, of carbon monoxide, or hypoxic encephalopathy may adversely affect the central nervous system as well as arterial hypertension [14, 23, 24, 26]. Other factors include hypo/hypernatremia, hypovolemic shock, sepsis, antibiotic over-dosage (e.g., penicillin), and possible over-sedation or withdrawal effects of sedative drugs. If increased intracranial pressure is suspect neurosurgery consuilt has to be coducted to be assessed for ICP monitoring and bolt palcement to treat increased intracranial pressure.

In general, severe burn injury is associated with nonspecific atrophy of the brain that normally resolves over time. No intervention is needed.

Pain and anxiety will generally require rather large doses of opioids and sedatives (benzodiazepines mainly). Continuous infusion regimens will generally be successful in maintaining pain within acceptable ranges. Sedatives and analgesics should be targeted to appropriate sedation and pain scales (SAS or VAS scores 4 appear optimal). Thus preventing the sequelae associated with over-sedation and opioid creep, namely fluid creep and effects on the central and peripheral cardiovascular system [18]. Therefore, consideration should be given to the use of NMDA receptor antagonist, such as ketamine or gabapentin, who have important opioid sparing effects to decrease the need for opioids and benzodiazepines [2, 4]. We find multimodal pain management combining a long-acting opioid for background pain, a short-acting opioid for procedures, an anxiolytic, an NSAID, Acetaminophen, and Gabapentin for neuropathic pain control [2, 4] used at our institution targeted to SAS (sedation score) and VAS (visual analog scale) scores provide adequate analgesia and sedation.

3.1.1 Intensive Care Unit-Acquired Weakness

Survival and organ function have been the main outcome measures for burn patients; however, recently long-term outcomes move into the focus of burn care providers. A significant component of long-term outcomes include the peripheral nervous system and muscular system which manifest as neuromyopathy. The importance of positioning and prevention of peripheral nerve compression is well known and ingrained in the daily practices of most critical care units. The main risk factors for neuropathy include: multiple organ failure, muscular inactivity, hyperglycemia, use of corticosteroids, and neuromuscular blockers. In a recent publication by de Jonghe et al. [31], early identification and treatment of conditions leading to multiple organ failure, especially sepsis and septic shock, avoiding unnecessary deep sedation and excessive hyperglycemia, promoting early mobilization, and weighing the risk and benefits of corticosteroids might reduce the incidence and severity of ICU acquired weakness.

3.1.2 Thermal Regulation

Temperature regulation is altered with a “resetting” of the hypothalamic temperature above nor-

mal values [32–34]. The teleological advantage of maintaining an elevated core temperature following burn injury is not fully understood, but major burns destroy the insulating properties of the skin, while the patients strive for a temperature of 38.0–38.5 °C. Sometimes, it is difficult to differentiate elevated temperatures due to a central reset or due other causes such as infection or fever. Our protocol call for cultures if temperatures are persistently over 39 °C.

Catecholamine production contributes to the changes in association with several cytokines, including interleukin-1 and interleukin-6. Any attempt to lower the basal temperature by external means will result in augmented heat loss, thus increasing metabolic rate. Ambient temperature should be maintained between 28 and 33 °C to limit heat loss and the subsequent hypermetabolic response [3]. Metabolic rate is increased as a consequence of several factors such as the catecholamine burst, the thermal effects of proinflammatory cytokines and evaporative losses from the wounds, which consumes energy, causing further heat loss. The evaporation causes extensive fluid losses from the wounds, approximating 4000 ml/m^2/%TBSA burns [2, 4]. Every liter of evaporated fluid corresponds to a caloric expenditure of about 600 kcal.

Beside hyperthermia, another very important contributor to poor outcome is hypothermia. Burn patients frequently experience hypothermia (defined as core temperature below 35 °C) on admission, on the ICU, during OR, during sepsis [2, 4]. Time to recover from hypothermia has been shown to be predictive of outcome in adults, with time to revert to normothermia being longer in non-survivors. Considering that hypothermia favors infections and delays wound healing, the maintenance of peri-operative normothermia is of utmost importance. Tools include warming the ambient room temperature, intravenous fluid warming systems, and warming blankets. The temperature of the bed should be set at 38 ± 0.5 °C. However, this is contraindicated in the febrile patient, as it complicates fluid therapy due to largely unpredictable free water losses, and respiratory management due to the supine position. The patient may require additional 1–4 l of free water per day (as D5W IV or enteral free water) to prevent dehydration. These additional requirements are difficult to assess in the absence of bed-integrated weight scales. This further exposes the gut to dehydration with subsequent constipation.

3.2 Heart

The typical complication in severely burned patients is cardiomyopathy requiring inotrope therapy, which was discussed above.

Another complication that can occur is cardiac ischemia. Ischemic events can lead to a manifest heart or to temporary cardiac ischemia. If a heart attack occurs (ECG, Trops, CK, clinical symptoms), cardiology should be immediately involved and guide therapy that usually includes Aspirin, Beta-blocker, and Nitro. Cardiology can also refer the patient to interventional cardiology for an angio.

3.3 Lung

Pulmonary complications in the early phase are pulmonary edema and inhalation injury that was discussed above. A pulmonary problem that occurs during ICU or hospital stay is VAP (ventilation associated pneumonia)/Pneumonia and ARDS.

3.3.1 Ventilator-Associated Pneumonia

The ABA guidelines for prevention, diagnosis, and treatment of ventilator-associated pneumonia (VAP) in burn patients were published in 2009 [15, 35]. The guidelines are as follows:

- Mechanically ventilated burn patients are at high risk for developing VAP, with the presence of inhalation injury as a unique risk factor in this patient group.
- VAP prevention strategies should be used in mechanically ventilated burn patients.
- Clinical diagnosis of VAP can be challenging in mechanically ventilated burn patients where

systemic inflammation and acute lung injury are prevalent. Therefore, a quantitative strategy, when available, is the preferable method to confirm the diagnosis of VAP.
- An 8-day course of targeted antibiotic therapy is generally sufficient to treat VAP; however, resistant *Staphylococcus aureus* and Gram-negative bacilli may require longer treatment duration.
- Any effort should be made to reduce length of intubation.

Our policy is to administer antibiotics according to the length of hospitalization. Patients admitted within the past 5 days should be started on an empiric regimen of:

- Ceftriaxone 1 g iv q24h +/− cloxacillin 1–2 g iv q4-6h.

Penicillin Allergy:

- Levofloxacin 750 mg iv/po q24h.

Late Phase (Admitted >5 days):

- Piperacillin/tazobactam 4.5 g iv q6h (renal dosing required).
- +/− vancomycin 1 g iv q12h (with pre- and post-levels around the third dose).

Penicillin allergy
- Tobramycin 2 mg/kg q8h (in non-obese patients with crcl >70 ml/min; + vancomycin 1 g iv q12h (with pre- and post-levels around the third dose).
- or,
- meropenem 500 mg iv q6h (renal dosing required).

3.4 Liver/GI

Severe burn injury causes numerous metabolic alterations, including hyperglycemia, lipolysis, and protein catabolism [3, 6, 36]. These changes can induce multi-organ failure and sepsis leading to significant morbidity and mortality [36–38]. Liver plays a significant role in mediating survival and recovery of burn patients, and preexisting liver disease is directly associated with adverse clinical outcomes following burn injury [39–41]. In the study by Price et al. in 2007, they demonstrated that preexisting liver disease increased mortality risk from 6% to 27%, indicating that liver impairment worsens the prognosis in patients with thermal injury. Severe burn also directly induces hepatic dysfunction and damage, delaying recovery. More recently, work by Jeschke et al. (2009) and Song et al. (2009) has shed light on the mechanism of the hepatic dysfunction following thermal injury, mainly by the up-regulation of the ER stress response, and increased cell death contributing to compromised hepatic function post-burn [42–47]. Thus, one must not only be cognizant of the significant deleterious effects of hepatic dysfunction in the thermally injured patient as it has significant consequence in terms of multi-organ failure, morbidity, and subsequent mortality of these patients; one can focus therapeutic modalities to alter this response and possibly improve outcome.

3.4.1 GI Complications/GI Prophylaxis/Enteral Nutrition

The effect of thermal injury on the gastrointestinal system was identified in 1970 by Dr Basal Pruitt with the description of Curling's ulcer. During the initial hours, splanchnic blood flow is reduced, except for flow to the adrenals and to the liver. Poorly perfused organs shift towards anaerobic metabolism leading to acidosis. Adequate fluid resuscitation restores perfusion to a great extent. But with over-enthusiastic fluid delivery, increasing intra-abdominal pressures and consequently abdominal compartment syndrome (ACS) becomes a matter of concern in both adult and pediatric burn patients [19, 48]. The Ivy index (250 ml/kg fluid resuscitation) is a cut-off value beyond which trouble is nearly certain. Abdominal pressures start rising, soon reaching the "gray zone" of 15–20 mmHg, and then the danger zone >20 mmHg, beyond which medical

measures must be taken to reduce the IAP to avoid splanchnic organ ischemia. IAP monitoring is essential for TBSA >30%. Abdominal compartment syndrome is a complication that is associated with high mortality and in general laparotomy should be avoided. Abdominal pressure should be controlled by diuresis, sedation, and even paralytics if needed. If the abdomen is burned, checker-board escharotomies need to be performed.

The gut is extremely vulnerable to changes in perfusion and nutrition. Even short ischemia can lead to gut atrophy associated with several complications. Early enteral feeding should be initiated no later than 12 h after injury. The benefits of this strategy are numerous: increasing blood flow to the splanchnic compartment before edema makes it impossible, maintaining pyloric function, maintaining intestinal motility, and reducing significantly infectious complications. Current recommendations are to place a nasogastric feeding tube as well as post-pyloric feeding tube.

During the initial phase post-burn as well as after each ischemia-reperfusion hit gastrointestinal function, including pyloric function, is vastly depressed. A true paralytic ileus will ensue for many days if the gastrointestinal tract is not used. Opiates and sedatives, further depress the gastrointestinal function and constipation is frequent and may become critical with the development of ileus and intestinal obstruction by feces. Prevention should be initiated from admission using fiber containing enteral diets, lactulose (osmotic cathartic), and enemas when the other measures have failed. Regular bowel movements need to be diligently monitored.

Gut complications may be life-threatening: in addition to the already-mentioned ACS and constipation, the patients may develop Ogilvie syndrome, ischemic and nonischemic bowel necrosis, and intestinal hemorrhage. A careful tight supervision of bowel function with daily examinations is therefore mandatory, particularly in peri-operative periods with intra-operative hemorrhage leading to hypovolemia, which exposes the patient to gut hypo-perfusion and their threatened complications.

Stress ulcer prophylaxis is mandatory, usually by H2-blockers (ranitidine) or proton pump inhibitors) since the bleeding risk is elevated in burn injuries and may be life-threatening.

3.4.2 Micronutrients and Antioxidants

Critically ill-burned patients are characterized by a strong oxidative stress, an intense inflammatory response, and a hypermetabolic state that can last months. Trace element (TE) deficiencies have repeatedly been described. The complications observed in major burns, such as infections and delayed wound healing, can be partly attributed to TE deficiencies [49, 50]. Plasma TE concentrations are low as a result of TE losses in biological fluids, low intakes, dilution by fluid resuscitation, and redistribution from plasma to tissues mediated by the inflammatory response. The large exudative losses cause negative TE balances. Intravenous supplementation trials show that early substitution improves recovery (IV doses: Cu 3.5 mg/day, Se 400–500 mcg/day, Zn 40 mg/day), reduces infectious complications (particularly nosocomial pneumonia), normalizes thyroid function, improves wound healing and shorten hospital length of stay. The mechanisms underlying these improvements are a combination of antioxidant effects (particularly of selenium through restoration of glutathione peroxidase activity), but also immune (Cu, Se, Zn) and anabolic effects (Zn particularly).

High vitamin C requirements after major burns were identified already in the 40s and have been confirmed since. Very interesting studies by Tanaka et al. in 2000 and Kremer in 2010 demonstrated that high doses of vitamin C administered during the first 24 h after a major injury reduced the capillary leak, probably through antioxidant mechanisms, resulting in significant reductions in fluid resuscitation requirements [51, 52].

3.5 Renal

Acute renal failure (ARF) is a major complication of burn injury. The incidence of ARF in burned patients ranges from 1.2 to 20% and the

incidence of ARF requiring renal replacement therapy (RRT) from 0.7% to 14.6% [8, 53–55]. Although ARF is relatively rare, early diagnosis is important, as the mortality of burn patients with manifest ARF has been reported around 50% [53]. Applying the RIFLE classification to burn patients, Coca et al. found that the incidence of acute kidney injury was 27%, and it carried with it a mortality rate of 73% in the patients with the most severe acute kidney injury (requiring dialysis).

Burn-related ARF can be divided into early and late ARF, depending on the time of onset with each having different etiologies [55, 56]. Early ARF occurs during the first 5 days post-burn and its main causes are hypovolemia, hypotonia, and myoglobinuria. Prevention focuses on early aggressive fluid resuscitation and escharotomies or fasciotomies. Late ARF begins more than 5 days post-burn and is usually multifactorial (generally caused by sepsis and/or nephrotoxic antibiotics) [56].

Regardless of the cause, there is recent strong evidence that renal replacement therapy (RRT) should be instituted as early as possible in burn patients with renal dysfunction before the traditional criteria for RRT has been established. A recent multicenter study indicated to start RRT with high flow as soon as possible AKI manifests itself [57]. The early initiation of RRT improves outcomes of burn patients.

Further to the discussion of RRT is the choice in mode of delivery. CRRT (continuous renal replacement therapy) offers several potential advantages in the management of severe acute renal failure in burn patients. It is slow and continuous, consequently allowing for very efficient metabolic clearance and ultra-filtration of fluids, while minimizing hemodynamic compromise. Thus allowing for ongoing optimization of fluid and metabolic management. Hemodialysis is surely a viable option if the patient tolerates it. In children, an alternative is peritoneal dialysis with placement of a Tenckhoff catheter.

3.6 Hormonal (Thyroid, Adrenal, Gonadal)

In the post-burn state, pronounced hormonal and metabolic changes take place [3, 6], starting immediately after injury. There is a tremendous increase in stress hormones after major burns, the increase being particularly marked during the first 2–3 weeks, but the alterations will persist for months and even years [39]. In response to the afferent stimuli from the burn wound, an intense sympatho-adrenal response is elicited. Catecholamine secretion contributes to arterial pressure maintenance, but also to a massive increase in cardiac after-load. The concentration of epinephrine and norepinephrine remains elevated for several days after injury and contributes to the integrated neuro-endocrine stress response. Cortisol increases markedly, and the intensity of the response is modulated by optimization of pain control with good analgesia [6, 39]. As with many other hormones, the circadian rhythm also changes. Aldosterone levels increase for several days. ACTH response frequently parallels the cortisol levels and tends to be elevated for a few weeks. The increase in plasma rennin activity and aldosterone persist for several weeks.

A patient suffering from infection/sepsis or persistent hypotension should be considered for possible adrenal insufficiency. Previous guidelines called for a baseline cortisol level and if that level is low an ACTH challenge test should be performed to rule out insufficiency. If an adrenal insufficiency is present, low-dose cortisol should be given. Newer guidelines call for a test dose of cortisol and see whether blood pressure and symptoms improve with this test dose. If there is an improvement, short-term steroid administration should be considered.

Glucagon concentration is also increased after burn injury, contributing heavily to the hypermetabolic response, while insulin tends to remain within normal values, being paradoxically normal while plasma glucose concentration is elevated.

The thyroid axis exhibits major abnormalities in the patients with major burns. The most constant finding is a "low T3 syndrome": TSH is generally normal, with low T3 levels, and T4 levels in the low-normal values, with elevated rT3 levels reflecting an altered de-iodination at the hepatic level. If a low T3 is present, there are two options: to administer selenium because selenium deficiency is associated with low T3 levels, and/or thyroid hormone should be replaced.

Post-burn the gonadal axis is depressed in any patient with major burns. In men, post-burn changes in testosterone and 17 beta-estradiol are greater than in females, even during the first days. Plasma testosterone also decreases steeply in limited burn injury. The alterations last at least 4–5 weeks, but may persist for months in critically ill-burned patients. The changes seem proportional to the severity of burns. A decreased pituitary stimulation causes lowered hormonal secretions from the testes. This change contributes to the low anabolic response and opens substitution perspectives. LH is more or less normal, LH-RH is decreased, FSH is low, and Prolactin is low to elevated.

In premenopausal females, amenorrhea is a nearly universal phenomenon, despite a near-normal 17 beta-estradiol plasma concentration. Progesterone levels remain very low for many months after injury. Testosterone response is very different from that of males, with nearly normal concentrations in young females, and normal response to ACTH which elicits an increase in testosterone, while it decreases in men. Prolactin levels are also higher than seen in men.

In children, despite adequate nutritional support, severe thermal injury leads to decreased anabolic hormones over a prolonged period of time (Jeschke et al. 2005). These changes contribute to stunting of growth observed after major burns. Female patients have significantly increased levels of anabolic hormones, which are associated with decreased pro-inflammatory mediators and hypermetabolism, leading to a significantly shorter ICU length of stay compared with male patients.

3.7 Electrolyte Disorders

Burns is a condition where nearly any electrolyte abnormality can be observed. The causes for these disturbances are many and include fluid resuscitation with crystalloids, exudative and evaporative losses, impaired renal regulation, and responses to counterregulatory hormones.

3.7.1 Sodium

During the first 24 h, patients receive major amounts of sodium with their fluid resuscitation. Sodium accumulates in the interstitial space with edema. Despite this, hypernatremia occurring during the first 24 h reflects under-resuscitation and should be treated with additional fluid. Thereafter, mobilization of this fluid during the first weeks frequently results in hypernatremia, and its resolution requires free water. Hypernatremia may also result from persistent evaporative losses from the wounds, particularly in case of treatment on a fluidized bed (contraindicated with severe hypernatremia) or in case of fever. Hypernatremia may also herald a septic episode.

3.7.2 Chloride

During the early resuscitation and the surgical debridements of the burn wound, the patients tend to receive significant amounts of NaCl resulting in hyperchloremic acidosis. The excess chloride is difficult to handle for the kidney, but the condition is generally resolves without further intervention.

3.7.3 Phosphate and Magnesium

Burns have high requirements for phosphate and magnesium in the absence of renal failure. Those requirements start early and are largely explained by two mechanisms: large exudative losses and increased urinary excretion associated with acute protein catabolism and stress response. Stimulation of sodium excretion is usually required and can usually be achieved by the simultaneous administration of free water (D5W IV or enteral water) along with furosemide with or without thiazide diuretics.

3.7.4 Calcium

Total plasma calcium concentration consists of three fractions: 15% is bound to multiple anions (sulfate, phosphate, lactate, citrate), about 40% is bound to albumin in a ratio of 0.2 mmol/l of calcium per 10 g/l of albumin, the remaining 45% circulating as physiologically active ionized calcium. Calcium metabolism is tightly regulated. As albumin levels vary widely in burns and only ionized calcium is biologically active, only ionized calcium is a true indicator of status, as total plasma calcium determination is not a reliable indicator of calcium status: the use of conversion formula is unreliable:

$$[\mathrm{Ca}]\mathrm{calculated} = \mathrm{Total}[\mathrm{Ca}]\mathrm{measured} + \left(0.2 \times \left(45 - [\mathrm{albumin}]\right)\right)$$

Hypocalcemia may occur during the early resuscitation phase or in the context of massive peri-operative blood transfusion and requires intravenous supplementation using any form of available intravenous calcium formulation. Hypercalcemia remains a poorly recognized cause of acute renal failure in patients with major burns that occurs as early as 3 weeks after injury. The triad of hypercalcemia, arterial hypertension, and acute renal failure is well known in other critical illnesses, while the association of hypercalcemia and renal failure in patients with major burns is much less reported in the literature. In a recent retrospective study, hypercalcemia was shown to occur in 19% of the burned patients with hospital lengths of stay of more than 28 days and was noted to be associated with an increased mortality. Hypercalcemia may also occur in patients with smaller burns requiring a stay of more than 20 days in the ICU. Ionized calcium determination enabled earlier detection, while using total calcium determination "with albumin correction" was only slightly sensitive, as shown by normal corrected values in 15 cases with ionized hypercalcemia. The treatment of hypercalcemia includes hydration, volume expansion, and early mobilization. As most causes of severe hypercalcemia depend on increased osteoclast activation, drugs that decrease bone turnover are effective. The treatment of choice in cases that do not resolve with the simple measures relies on the bisphosphonates, pamidronate disodium, and zoledronic acid, which are available in intravenous forms. In burned children, acute intravenous pamidronate administration has been shown to help to preserve bone mass, achieving a sustained therapeutic effect on bone [58]. An alternative treatment of the latter in burns includes anabolic agents such as oxandrolone [59]. The bisphosphonates have been advocated in the prevention of heterotrophic ossification, a complication that occurs in 1.2% of burn patients.

3.8 Bone Demineralization and Osteoporosis

Due to the substantial alterations of calcium and phosphorus metabolism and bone formation is reduced both in adults and children when burns exceed 40% TBSA. Bone mineral density is significantly lower in burned children compared with the same age normal children. Girls have improved bone mineral content and percent fat compared with boys [6, 60, 61]. The consequences are increased risk of fractures, decreased growth velocity and stunting. The bone is affected by various means: alteration of mineral metabolism, elevated cytokine and corticosteroid levels, decreased growth hormone (GH), nutritional deficiencies, and intra-operative immobilization. Cytokines contribute to the alterations, particularly interleukin-1 beta and interleukin-6, both of which are greatly increased in burns and stimulate osteoblast-mediated bone resorption. The increased cortisol production in thermal injury leads to decreased bone formation, and the low GH levels fail to promote bone formation [62], further exacerbating the situation. Various studies suggest that immobilization plays a significant role in the pathogenesis of burn-associated bone disease. Alterations of magnesium and calcium homeostasis constitute another cause. Hypocalcemia and hypomagnesemia are constant findings, and ionized calcium levels remain low for weeks. The alterations are partly explained by large exudative magnesium and phosphorus losses. A close monitoring of ionized

calcium, magnesium, and inorganic phosphate levels is mandatory since burn patients usually require substantial supplementation by intravenous or enteral routes.

3.9 Coagulation and Thrombosis Prophylaxis

The coagulation and hematologic system is profoundly affected by a burn and the associated changes vary from depletion to overproduction. These acute phase responses are normal for a burn injury and usually require no major or only minor intervention. Hematological alterations observed after burns are complex and can last for several months and can be summarized as follows:

- During the early phase after burns, fibrin split products increase.
- Dilution and consumption explain the early low PT values.
- The coagulation cascade is activated.
- Fibrin, factors V and VIII increase as part of acute phase response.
- Antithrombin deficiency is frequent.
- Thrombocytosis develops when wounds are closing.

The risk of deep venous thrombosis and of pulmonary embolism is at least as high as in any other surgical condition. In our experience, 13% of patients develop some form of thrombotic complication. Specific risk factors include central venous lines, prolonged bed-rest, and an intense inflammatory state. Prophylaxis should be started from admission. Interruptions for surgery should be reduced to minimum and discussed with the surgical team.

4 Conclusion

The management of the critically ill thermally injured patient can be very complex. The treatments modalities can remain at times controversial, as there is a lack of high-level evidence. There have been many advances in the field of the critical care of the thermally injured patient, which would benefit from large-scale multicenter trials. This brief chapter highlights few of the important nuances in the care of these patients and places emphasis on the need for intricate support for the all organ systems in order to improve morbidity and mortality.

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Infections in Burns

Shahriar Shahrokhi

1 Burn Wound Infections

1.1 Diagnosis and Treatment of Burn Wound Infections

1.1.1 Introduction

Infections remain a leading cause of death in burn patients. This is as a result of loss of the environmental barrier function of the skin predisposing these patients to microbial colonization leading to invasion. Therefore, reconstitution of the environmental barrier by debriding the devitalized tissue and wound closure with application of allograft versus autograft is of optimal importance.

Given that infections are a common complication of the thermally injured patient, early diagnosis, and treatment are of paramount importance. The pathophysiological progression of burn wound infection runs the spectrum from bacterial wound colonization to infection to invasive wound infection. The characteristics of each are as follows:

- *Bacterial colonization.*
  - Bacterial levels $<10^5$.
  - Does not necessarily prevent wound healing.
- *Bacterial infection.*
  - Bacterial levels $>10^5$.
  - Can result in impaired wound healing and graft failure.
  - Can lead to systemic infection.
- *Invasive wound infection.*
  - Clinically can have separation of the eschar from wound bed.
  - Appearance of focal dark brown, black, or violaceous discoloration of the wound [1].
  - Presence of pyocyanin (green pigment) in subcutaneous fat.
  - Erythema, edema, pain, and warmth of the surrounding skin.
  - Associated with signs of systemic infection/sepsis and positive blood cultures and high mortality.

Of note there are particular clinical signs unique to fungal and viral infections. An unexpected and rapid separation of the eschar is characteristic of fungal infection [2], while vesicular lesions caused by HSV-1 can be found in healed or healing burn wounds [3].

1.2 Common Pathogens and Diagnosis

In general, the organisms causing burn wound infection/invasion have a chronological appearance. Initially, Gram-positive organisms are com-

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monplace, while Gram-negative organisms become predominant after 5 days post-burn injury. Yeast and fungal colonization/infection follow, and finally multi-resistant organisms appear typically as a result of broad-spectrum antibiotics or inadequate burn excision or patient response to therapy [4].

As part of infection surveillance of burn patients, clinicians need to pay close attention to clinical signs of wound infection and rapidly confirm their diagnosis. There is some controversy as to the exact method of diagnosis, with some advocating for quantitative cultures—with $>10^5$ organisms per gram tissue being diagnostic of invasive infection [5]—and others arguing for histological examination as the only reliable method of determining invasive infection [6–9] since quantitative cultures are only positive in 50% of histological invasive wound infections [9]. The most common pathogens of burn wound invasion are MSSA, MRSA, and *Pseudomonas aeruginosa* species (Table 1).

In order to provide the thermally injured patient with adequate treatment, it is important to have knowledge of each institution's bacterial flora as they vary with geography and change over time [10, 11].

Fungal infections have increased in frequency with the use of topical agents, and the incidence of mycotic invasions has doubled. Even though the burn wound is the most commonly infected site, there is an increasing trend towards systemic and organ-specific fungal infections [12].

The diagnosis of fungal infection is complicated by delay in their identification as cultures typically require 7–14 days [13], and their clinical presentation is similar to low-grade bacterial infections. Diagnosis and duration of treatment can be aided by arterial blood samples as well as retinal examination.

1.3 Clinical Management

Early excision and wound coverage is the mainstay of modern burn care and the best method of minimizing burn wound infection. Any delay in the surgical treatment of burn wounds leads to increased bacterial loads, and any wound with bacterial counts exceeding 10^5 organisms per gram of tissue can develop burn wound sepsis even after burn wound excision [9].

The treatment of burn wound infections involves both local and systemic therapy.

1.3.1 Local

- Early excision of burn eschar (for unexcised burns).
- Aggressive excision of necrotic/infected tissue.
- Use of topical agents (Table 2) to minimize bacterial colonization [14].

Table 1 Common pathogens of burn wound infection

Organism	Common species
Gram-positive bacteria	*Staph* and *Strep* species
Gram-negative bacteria	*Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *E. coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*
Yeast	*Candida* sp.
Fungi	*Aspergillus*, *Penicillium*, *Rhizopus*, *Mucor*, *Rhizomucor*, *Fusarium* and *Curvularia*—Have greater invasive potential
Virus	HSV, CMV
Multi-resistant bacteria	MRSA, VRE, MDR *Pseudomonal* and *Acinetobacter* species

Table 2 Common topical agents and their antimicrobial activity

Agent	Effective against
Silver sulfadiazine	Gram-positives, Gram-negatives, yeast
Mafenide acetate (5%)	Gram-positives, Gram-negatives
Silver nitrate (0.5%)	Gram-positives, Gram-negatives, yeast, fungi
Acetic acid (0.5–5%)	Gram-positives, Gram-negatives, pseudomonas at higher concentration
Sodium hypochlorite (0.005–0.5%)	Gram-positives, Gram-negatives, yeast, fungi
Acticoat™ (Nanocrystalline silver)	Gram-positives, Gram-negatives, yeast, fungi, MRSA, VRE

The use of any particular topical agent should be based on suspected organism in the wound but is at times guided by the availability of the agent on hospital formulary. These are not a substitute for aggressive surgical management of wound infections.

1.3.2 Systemic

- Use of systemic antibiotics and antifungals should be reserved for patients demonstrating systemic signs of sepsis (see ABA criteria for definition of sepsis (Box 1)).
- Use of systemic prophylaxis can reduce the rate of surgical wound infections but can increase bacterial antimicrobial resistance [15].

Box 1 ABA Criteria for Definition of Sepsis [16]

Includes at least three of the following:

Temperature > 39° or < 36.5 °C.

Progressive tachycardia

- Adults >110 bpm.
- Children >2 SD above age-specific norms (85% age-adjusted max heart rate).

Progressive tachypnea

- Adults >25 bpm not ventilated. Minute ventilation >12 L/min ventilated.
- Children >2 SD above age-specific norms (85% age-adjusted max respiratory rate).

Thrombocytopenia (will not apply until 3 days after initial resuscitation)

- Adults <100,000/mcl.
- Children >2 SD below age-specific norms.

Hyperglycemia (in the absence of pre-existing diabetes mellitus)

- Untreated plasma glucose >200 mg/dL or equivalent mM/L.
- Insulin resistance—examples include:
- >7 units of insulin/h intravenous drip (adults)
- Significant resistance to insulin (>25% increase in insulin requirements over 24 h).

Inability to continue enteral feedings >24 h

- Abdominal distension.
- Enteral feeding intolerance (residual >150 mL/h in children or two times feeding rate in adults).
- Uncontrollable diarrhea (>2500 mL/day for adults or > 400 mL/day in children).

In addition, it is *required* that a documented infection (defined below) is identified:

- Culture-positive infection.
- Pathologic tissue source identified.
- Clinical response to antimicrobials.

Infections of burn wounds are typically found in patients with burns exceeding 20% TBSA and most commonly in the lower extremities [17]. However, there are no specific organisms associated with the site of infection [17]. Moreover, these infections can have dire consequences:

- Conversion of superficial to deeper burn wounds.
- Systemic infection and sepsis.
- Graft loss requiring further surgery for regrafting.
- Increased hospital length of stay.
- Conversion of donor sites requiring surgical debridement and grafting.
- Increased mortality, more so with yeast and fungal infection.

- Yeast species (*Candida*) are typically sensitive to fluconazole, while fungal infections would most likely require treatment with amphotericin or caspofungin (the use is for systemic infection, as wound infections require surgical debridement).
- Viral infections (typically HSV) require treatment with acyclovir.

Table 3 Ross Tilley Burn Centre guidelines for empiric antibiotic therapy

***Early phase* (*<5 days*)**
The most common pathogens (from any source) in the early phase of a patient's admission are:
Gram-positive
Staphylococcus aureus (~90% susceptible to cloxacillin)
Gram-negatives (95% susceptibility to ceftriaxone)
H. influenza
E. coli
Klebsiella spp.
Based on this data, septic patients admitted within the past 5 days should be started on an empiric regimen of:
Ceftriaxone 1 g IV q24h +/− Cloxacillin 1–2 g IV q4–6h (renal dosing required)
If penicillin allergy: Levofloxacin 750 mg IV/PO q24h
***Late phase* (*>5 days*)**
The most common pathogens (from any source) in the late phase of a patient's admission are:
Gram-positive
Staphylococcus aureus (only ~60% susceptible to cloxacillin)
Gram-negative (generally more predominant in the late phase)
Pseudomonas aeruginosa (>80% susceptible to piperacillin/tazobactam)
Based on this data, septic patients admitted for 5 days or more should be started on an empiric regimen of:
Piperacillin/tazobactam 4.5 g IV q6 h (renal dosing required)
+ Vancomycin 1 g IV q12 h (with pre- and post-levels around the third dose)
Or
Meropenem 500 mg IV q6 h (renal dosing required)

- The choice of antimicrobials needs to be based on each institution's antibiogram and tailored specifically to the organism (Table 3), i.e., narrow the coverage as soon as sensitivities become available.

1.4 Conclusion

Burn wound infection is an all too common complication of the thermally injured patient. These infections tend to have a chronological appearance and depend on burn size, depth, length of hospital stay, and geographical location. The common organisms remain *Staphylococcus* and *Pseudomonas*; however, more resistant strains are becoming prevalent. The clinician needs to be vigilant with surveillance of burn wounds and institute aggressive treatment of wound infection once clinical signs appear before systemic illness sets in. It is of utmost importance to have ongoing assessment of the unique flora of each institution in order to better utilize systemic therapy.

2 Ventilator-Associated Pneumonia

Ventilator-associated pneumonia (VAP) as defined by CDC (Center for Diseases Control) is an infection that occurs in a mechanically ventilated patient with an endotracheal or tracheostomy tube (traditionally >48 h after hospital admission) [18, 19]. The diagnosis of VAP in the thermally injured patient can be challenging, as fever, leukocytosis, tachycardia, and tachypnea can be present in these patients without infection. The sources of bacteria are typically the oropharynx and upper gastrointestinal tract [20–24]. The organisms also have a temporal pattern, community-acquired organisms (*Streptococcus pneumoniae* and *Haemophilus influenza*) are dominant in the early-phase VAP and Gram-negative and multi-resistant organisms (i.e., MRSA) are the common pathogens in late-stage VAP.

Regardless of the organisms, early antimicrobial treatment, guided towards the likely organism based on the onset of VAP (early vs. late) is beneficial in the overall outcome of the patients [25–30]. These broad-spectrum antimicrobials would need to be de-escalated as cultures and sensitivities become available [31–33].

As VAP is an increasing common complication with significant consequences, VAP prevention strategies need to be implemented and ABA

Box 2 American Burn Association Practice Guidelines for Prevention, Diagnosis, and Treatment of Ventilator-Associated Pneumonia (VAP) in Burn Patients [34]

- Mechanically ventilated burn patients are at high risk for developing VAP, with the presence of inhalation injury as a unique risk factor in this patient group.
- VAP prevention strategies should be used in mechanically ventilated burn patients.
- Clinical diagnosis of VAP can be challenging in mechanically ventilated burn patients where systemic inflammation and acute lung injury are prevalent. Therefore, a quantitative strategy, when available, is the preferable method to confirm the diagnosis of VAP.
- An 8-day course of targeted antibiotic therapy is generally sufficient to treat VAP; however, resistant *Staphylococcus aureus* and Gram-negative bacilli may require longer treatment duration.

guidelines (Box 2) utilized to improve overall patient outcome.

3 Central Line-Associated Infections

Central catheters inserted into veins and arteries are common practice in the management of the critically ill thermally injured patient and can be associated with infection rates from 1.5 to 20% [35–37]. The introduction of central line insertion bundles by CDC has dramatically reduced these infections [38, 39]. These measures include:

- Hand washing.
- Full-barrier precautions during line insertion.
- Cleaning the skin with chlorhexidine.
- Avoiding the femoral site if possible.
- Removing unnecessary catheters.

In burn patients, some unique features complicate the use of the central catheters. Typically, there are associated burn wounds in close proximity, and it has been shown that catheters within 25cm^2 of an open wound are at an increased risk of colonization and infection [40]. Other risk factors associated with increased rate of infection are [41]:

- Age (extremes of age have more infection).
- Sex (female).
- %TBSA burned
- % full-thickness burns
- Presence of smoke inhalation.
- Type of burn (flame).
- Number of surgical procedures performed.
- Larger number of CVCs.
- Longer insertion of the catheter.
- Wound burn infection or colonization.
- Insertion of the venous catheter in emergency situation.
- Longer stay in hospital.
- More operations.
- Insertion site near the burns wound.

The diagnosis of catheter-related infection (CRI) is based on clinical and microbiological criteria (see Table 4). Following the diagnosis of CRI, prompt treatment is essential as delay in catheter removal or in the start of appropriate antimicrobial therapy can result in increased morbidity and mortality [43].

Currently, there is no clear evidence that routine exchange of lines decreases the rate of catheter-related blood stream infections (CRBSI) [44]; however, all catheters need to be removed once a CRBSI is diagnosed or once they are no longer needed.

As with all severe infections, empiric antimicrobial treatment should be initiated immediately and should take into account the severity of the illness, the site of catheter insertion, and the institutions' antibiogram [45]. These broad-spectrum antimicrobials need to be de-escalated after identification and susceptibility testing of the microorganism.

Table 4 Catheter-related infection [42]

Type of infection	Criteria
Catheter colonization	A significant growth of a microorganism from the catheter tip, subcutaneous segment, or catheter hub in the absence of clinical signs of infection
Exit-site infection	Microbiologically documented exudates at catheter exit site yield a microorganism with or without concomitant bloodstream infection.
	Clinically documented erythema or induration within 2 cm of the catheter exit site in the absence of associated bloodstream infection and without concomitant purulence
Positive blood culture	Microorganism, potentially pathogenic, cultured from one or more blood culture
Bloodstream infection	Positive blood culture with a clinical sepsis (see below)
Clinical sepsis	Requires one of the following with no other recognized cause: Fever (>38 °C), hypotension (SBP <90 mmHg), oliguria, paired quantitative blood cultures with a > 5:1 ratio catheter versus peripheral, differential time to positivity (blood culture obtained from a CVC is positive at least 2 h earlier than a peripheral blood culture)

4 Guidelines for Sepsis Resuscitation

As described in the previous segments of this chapter, infections in the thermally injured patient have dire consequences. Sepsis occurs at a rate of 8–42.5% in burn patients with a mortality of 28–65% [46]. Much research has been conducted in the optimal management of the septic patient. The following Table 5 summarizes the guidelines as recommended by the surviving sepsis campaign committee originally published in 2008 [47] and later revised in 2016 [48]. Only the strong recommendations with high level of evidence are included. This is to be used as a tool to guide the delivery of optimal clinical care for patients with sepsis and septic shock.

Table 5 Guidelines for management of sepsis and septic shock [48][a]

Initial resuscitation
• Sepsis and septic shock are emergencies—Treatment should start immediately
• Give 30 ml/kg IV crystalloid within 3 h for hypoperfusion
• Ongoing fluid resuscitation depends on reassessment of hemodynamic status
• If clinical exam not helpful, assess cardiac function
• Use dynamic variables to assess hemodynamic status
• Aim for MAP ε65mmHg when using pressors
• Aim to lower lactate to normal levels
Diagnosis
• Cultures should be obtained before starting antimicrobial therapy
Antimicrobial therapy
• Start IV antimicrobials within one hour of diagnosis of sepsis and septic shock
• Empiric broad-spectrum therapy should cover likely pathogens
• Narrow coverage once pathogens are identified and sensitivities are established, or clinical improvement
• Recommend against sustained antimicrobial prophylaxis in patients with severe inflammatory states (burns, pancreatitis)
• Optimize dosing based on pharmacokinetic and pharmacodynamic principles
• Start empiric combination therapy (at least two of different classes) aimed at likely organisms for septic shock
• Do not use combination therapy for other serious infections (sepsis, bacteremia)
• Do not use combination therapy for neutropenic sepsis
• De-escalate combination therapy within first few days in response to improvement for septic shock
• Treatment for 7–10 days is adequate for most infections causing sepsis/septic shock
• Longer courses are appropriate in patients with slow response, undrainable foci of infection, bacteremia with *S. aureus*, some fungi or viruses, or immunologic deficiencies
• Shorter courses are appropriate for patients with rapid resolution following source control
• Daily assessment for de-escalation
• Procalcitonin can be used to shorten therapy
• Procalcitonin can be used to support discontinuation of antibiotics
Source control
• Search for a diagnosis that can be treated with source control (i.e., abscess, infected wound)
• Remove intravascular access devices that could be a cause of sepsis as soon as possible (change lines)

Vasoactive medications
- Norepinephrine is the first choice for vasopressor
- Add vasopressin (up to 0.03 units/min) or epinephrine to norepinephrine next
- Use dopamine only in highly selected patients (low risk for tachyarrhythmias and bradycardia)
- Do not use dopamine for renal protection
- Use dobutamine in patients with persistent hypoperfusion despite adequate volume status and use of vasopressors
- Arterial lines should be placed if on vasopressors

Fluid therapy
- Continue fluid challenges as long as hemodynamic factors improve
- Use crystalloids as fluid of choice for initial resuscitation and subsequent volume replacement
- Use balanced crystalloids or saline for fluids
- Add albumin to crystalloids when patients require large volumes
- Do not use hydroxyethyl starches
- Crystalloids are preferred over gelatins

Corticosteroids
- Do not use steroids if fluids and vasopressors are effective. If not, IV hydrocortisone at 200 mg/day

Blood products
- Transfuse blood only when hemoglobin <7.0 mg/dL (except in extenuating circumstances—Myocardial ischemia, severe hypoxemia, acute hemorrhage)
- Do not use erythropoietin for anemia
- Do not use fresh frozen plasma to correct clotting abnormalities in the absence of bleeding or planned invasive procedure
- Transfuse platelets when <10,000/mm^3, and when <20,000 mm^3 if at risk for bleeding, ≥50,000mm^3 for active bleeding, surgery, or invasive procedures

Immunoglobulins
- Do not use IV immunoglobulins for sepsis/septic shock

Anticoagulants
- Do not use antithrombin for sepsis/septic shock

Mechanical ventilation (for sepsis-induced ARDS in adults)
- Target tidal volume of 6 mL/kg predicted body weight (not 12 mL/kg) 2. Use upper limit goal for plateau pressures of 30 cm H_2O
- Use higher PEEP over lower PEEP
- Use recruitment maneuvers
- Use prone position over supine if P/F < 150
- Do not use high-frequency oscillatory ventilation
- No recommendation about noninvasive ventilation
- Use neuromuscular blocking agents for ≤48 h if P/F < 150
- Use a conservative fluid strategy if no hypoperfusion
- Do not use β-2agonists if no bronchospasm
- Do not use a pulmonary artery catheter for sepsis-induced ARDS in adults
- Use lower tidal volumes in sepsis-induced respiratory failure without ARDS
- Elevate the head of bed to 30°–45° in ventilated patients
- Use spontaneous breathing trials in ventilated patients
- Use weaning protocols in patients who can tolerate weaning

Sedation and analgesia
- Minimize continuous or intermittent sedation in ventilated patients

Glucose control
- Use a protocol for glucose control when two consecutive glucose >180 mg/dL
- Monitor glucose every 1–2 h until stable, then every 4 h if on insulin infusion
- Interpret point-of-care glucose with caution
- Use arterial over capillary blood if arterial line present

Renal replacement therapy
- Use either continuous or intermittent renal replacement therapy
- Use continuous renal replacement therapy if hemodynamically unstable
- Do not use renal replacement therapy just for increased creatinine or oliguria without other definitive indications for dialysis

Bicarbonate therapy
- Do not use sodium bicarbonate with lactic acidemia with pH ≥ 7.15

Venous thromboembolism prophylaxis
- Use pharmacologic prophylaxis (UFH or LMWH) in the absence of contraindications
- Use LMWH rather than UFH
- Combine pharmacologic prophylaxis and mechanical prophylaxis whenever possible
- Use mechanical prophylaxis when pharmacologic prophylaxis is contraindicated

Stress ulcer prophylaxis
- Give stress ulcer prophylaxis to patients at risk for GI bleeding
- Use either proton pump inhibitors or histamine-2 receptor antagonists
- Do not use stress ulcer prophylaxis in patients without risk factors for GI bleeding

Nutrition
- Do not use parenteral feedings if enteral feedings possible
- Do not provide parenteral nutrition for the first 7 days if enteral feedings not possible (advance enteral feedings as tolerated)
- Start early enteral feedings if possible
- Start early trophic/hypocaloric or early full feedings (advance as tolerated)
- Do not use omega-3 fatty acids
- Do not check routine gastric residual volumes (but check if feeding intolerance or high risk for aspiration—applies to nonsurgical patients)

[a]Adapted from Rhodes et al. [48]

The ABA criteria for definition of sepsis (see Box 1) in the burn patients have been established. However, Mann-Salinas and colleagues have challenged the predictive ability of ABA criteria demonstrating that their multivariable model (heart rate > 130, MAP <60 mmHg, base deficit <−6 mEq/L, temperature < 36 °C, use of vasoactive medications, and glucose >150 mg/dL) is capable of outperforming the ABA model [49]. In addition, the new Sepsis-3 clinical criteria for identification of sepsis and septic shock [50–52] have been developed, which defines sepsis and septic shock as follows:

- **Sepsis—**Suspected or documented infection and an acute increase of >2 SOFA points.
- **Septic Shock—**Sepsis and vasopressor therapy needed to elevate MAP >65 mmHg and lactate >2 mmol/L (18 mg/dL) despite adequate fluid resuscitation.

More recently, the publication by Stanojcic and colleagues as well as Yan and colleagues demonstrated that the Sepsis-3 had superior sensitivity in predicting sepsis in comparison to Mann-Salinas and ABA criteria for sepsis; however, none of the aforementioned had the accuracy to be a stand-alone diagnostic tool within the burn population [53, 54].

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Wound Healing and Wound Care

Margarita Elloso and Gerd G. Gauglitz

1 Introduction

Understanding burn injury and its complex wound healing cascade requires recognition of the anatomy and physiology of the skin. The skin is a bilayer organ with many protective functions essential for survival.

The outer epidermal layer functions as a critical barrier composed of dead cells and keratin, which protects against bacterial and environmental toxins. The basal epidermal layer is the innermost layer of the epidermis that proliferate and divide to give rise to new cells for other epidermal layers. The undulating surface of the epidermis, called rete pegs, increases adherence of the epidermis to the dermis via the basement membrane.

The inner dermal layer has a number of essential functions, including continued restoration of the epidermis. The dermis is divided into the papillary and reticular dermis. The papillary dermis is extremely bioactive in comparison to the reticular dermis.

Superficial partial burns generally heal faster than deeper partial-thickness burns due to difference in bioactivity within the dermis; the papillary component is lost in deeper burns.

The damage or loss to the normal skin barrier functions cause the following common sequelae after burn injury:

- infection,
- loss of body heat,
- increased evaporative water loss,
- change in key interactive functions such as touch and appearance,
- excessive scarring leading to contractures.

Scars form as a result of physiologic wound healing process and may arise following any insult to the deep dermis. Genetic susceptibility, specific anatomic location, prolonged inflammation and delayed epithelialization significantly increases risk of developing excessive scarring. Hypertrophic scarring forms frequently after burn injury with incidence rates varying from 40% to 91%, depending on the depth of the wound [1, 2].

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2 Physiological Versus Pathophysiologic Wound Healing

The physiologic response to an injury to the skin in adult tissue is the formation of a scar which can be temporally grouped into three distinct overlapping phases.

- inflammation,
- proliferation,
- remodeling [3–5].

Each phase is critical to the success of wound closure. Deviations from the norm may be associated with delayed or abnormal wound healing [6].

Immediately following wounding, platelet degranulation, and activation of the complement and clotting cascades form a fibrin clot for hemostasis, which acts as a scaffold for wound repair [3].

Platelet degranulation is responsible for the release and activation of an array of potent cytokines, such as epidermal growth factor (EGF), insulin-like growth factor (IGF-I), platelet-derived growth factor (PDGF), and transforming growth factor-beta (TGF-β), which serve as chemotactic agents for the recruitment of neutrophils, macrophages, epithelial cells, mast cells, endothelial cells, and fibroblasts [3, 7].

48–72 h after the initial event the healing process transitions into the proliferation phase which may last for up to 3–6 weeks [8]. Recruited fibroblasts synthesize a scaffold of reparative tissue, the so-called extracellular matrix (ECM). This granulation tissue is made of procollagen, elastin, proteoglycans, and hyaluronic acid and forms a structural repair framework to bridge the wound and allow vascular ingrowth [8]. Modified fibroblasts, the so-called myofibroblasts, containing actin filaments help initiating wound contraction.

Once the wound is closed, the immature scar can transition into the final maturation phase, which may last several months. The abundant ECM is then degraded and the immature type III collagen of the early wound can be modified into mature type I collagen [8] (Fig. 1).

- *The transformation of a wound clot into granulation tissue thus requires a delicate balance between ECM protein deposition and degradation, and when disrupted, abnormalities in scarring appear, resulting in excessive scar formation* [5].

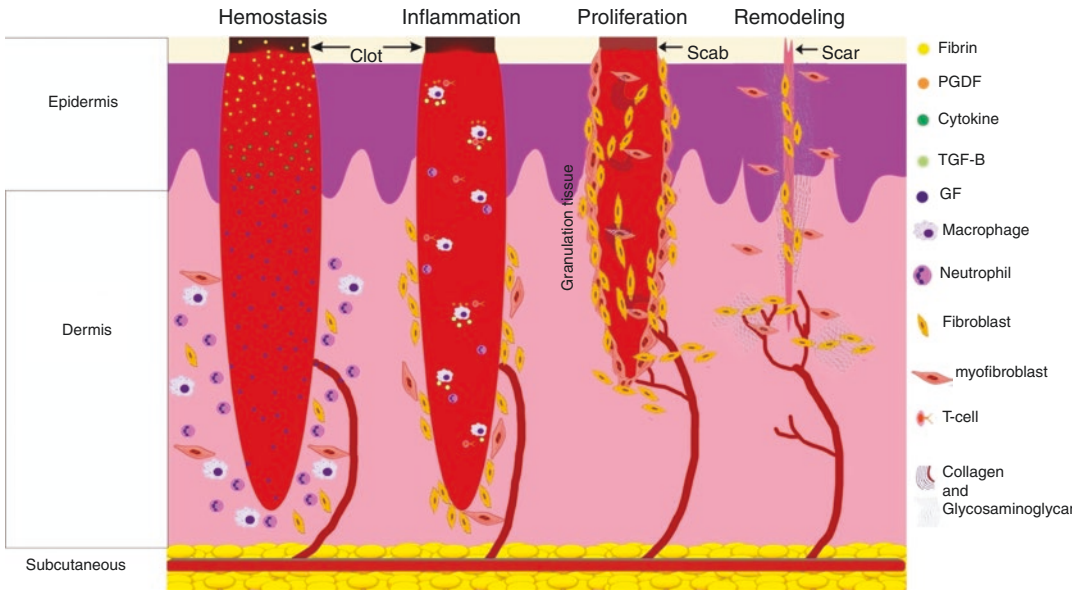

Fig. 1 Phases of wound healing

Recent evidence suggests that it is not simply the severity of inflammation that predisposes to excessive scarring but also the type of the immune response [9]. T-helper cells (CD41) cells have been implicated as major immunoregulators in wound healing.

The characteristic cytokine expression profile of the CD41 T cells represents the basis for describing either a predominantly Th1 or Th2 response to a specific or unspecific stimulus [5, 10].

While the development of a Th2 response (with production of interleukin (IL) -4, IL-5, IL-10, and IL-13) has been strongly linked to fibrogenesis, a predominance of Th1 CD41 cells has been shown to almost completely attenuate the formation of tissue fibrosis via production of interferon-gamma (IFN-γ) and IL-12 [11, 12].

2.1 Growth Factors

2.1.1 Transforming Growth Factor-Beta

Many of the biologic actions of TGF-β contribute to the normal wound healing process and have been implicated in a wide variety of fibrotic disorders [5]. Early after injury, high levels of TGF-β are being released from degranulating platelets at the site of injury, where they act as chemoattractants for lymphocytes, fibroblasts, monocytes, and neutrophils [13].

- The TGF-β family consists of at least five highly conserved polypeptides, with TGF-β1, −2, and −3 being the principal mammalian forms.
- TGF-β1 and −2 are one of the most important stimulators of collagen and proteoglycan synthesis and affects the ECM not only by stimulating collagen synthesis but also by preventing its breakdown [14, 15].
- TGF-β3, which is predominantly induced in the later stages of wound healing, has been found to reduce connective tissue deposition [16].
  - *Specifically, beyond 1 week, differential expression of TGF-β isoforms, receptors and activity modulators, rather than the mere presence or absence of TGF-β, may have a major role in the development of both, keloids and hypertrophic scarring* [17].

Interactions between keratinocytes and fibroblasts. Keratinocytes have been shown to mediate the behavior of fibroblasts during wound healing through their secretion, activation, or inhibition of growth factors such as TGF-β [9]. Particularly, release of IL-1 from keratinocytes at the wound site seems to represent the initial trigger for the inflammatory reaction and serves as an autocrine signal to fibroblasts and endothelial cells, resulting in a pleiotropic effect on them [18, 19].

2.1.2 Matrix Metalloproteinases (MMP)

The major effectors of ECM degradation and remodeling belong to a family of structurally related enzymes called MMP [5]. The MMP family consists of about 25 zinc-dependent and calcium-dependent proteinases in the mammalian system [20].

An imbalance in expression of MMPs has been implicated in a number of pathological conditions such as dermal fibrosis [21], tumor invasion and metastasis [22].

Several MMPs have been shown to mediate the breakdown of type I and III collagen, the most abundant types of collagen in the skin ECM [20]. Specifically, MMP-2 and MMP-9 activity persists after wound closure and seems to play a potent role in the remodeling process [23].

3 Wound Care Post-Burn

Treatment of burns depend on the characteristic, size, and depth of the wound. Treatments aim to expedite healing, prevent infection while minimizing patient discomfort. Burn wound therapies can be divided into three stages: assessment, management, and rehabilitation.

Management phase begins after the extent and depth of the wounds have been assessed and

wounds have been thoroughly cleaned and debrided.

Each wound should be dressed with appropriate covering that serves several purposes.

- First, it should protect the damaged epithelium, minimize bacterial and fungal colonization, and provide splinting action to maintain the desired position of function.
- Second, the dressing should be occlusive to reduce evaporative heat loss and minimize cold stress.
- Third, the dressing should provide comfort over the painful wound [24, 25].

The choice of dressing is based on the characteristics of the wound:

- First-degree wounds are minor and superficial with minimal loss of barrier function. These wounds require no dressing and are treated with topical salves to decrease pain and keep the skin moist.
- Superficial second-degree wounds will heal spontaneously, with minimal hypertrophic scarring, within 2–3 weeks if the wound remains free of infection. The capacity to heal is also dependent on the health and age of the individual. Older people and those with concomitant medical conditions are prone to delayed healing [26, 27]. These wounds need to be assessed daily and managed with dressings developed to aid in re-epithelialization, preventing wound infection, skin desiccation, and further skin damage.
- Deep second-degree and third-degree wounds will not heal and these wounds require excision and grafting.

Wound dressings can be categorized into four groups as seen in Table 1.

Table 1 Wound dressing categories

Dressing	Description	Disadvantage	Example
Conventional dressings [28, 29]	• Do not contain antibiotics or medications. • Widely used to cover clean burns to facilitate re-epithelialization	• Needs daily dressing change that can cause pain and discomfort	• Paraffin gauze • Vaseline gauze
Antiseptic and Antimicrobial dressings	• Dressings can be prepared as topical ointments or solutions • Can also be silver impregnated • Used to prevent wound infection by minimizing bacterial colonization	• Can be cytotoxic	• Sodium hypochlorite • Acetic acid • Polysporin • Povidone-iodine • Silver sulfadiazine • Aquacel AG • ACTICOAT
Biological dressings [30, 31]	• Effective in providing moisture and helps decrease bacterial load • have a more intact and native ECM structure which may allow the construction of a more natural new dermis	• Poor mechanical stability	• Amnion – Derived from human placenta
Biosynthetic dressings [32]	• Designed to use materials that simulate the function normal skin	• Expensive • Cannot be used for infected wounds • Cannot debride necrotic tissue	• Biobrane® – A temporary synthetic dressing composed of nylon mesh bonded to a silicone membrane, helps control water loss and re-epithelialization [33]. • TransCyte®

3.1 Burn Wound Excision

Methods in treating burn wounds have changed in recent decades. Most studies have shown that skin excision within 72 h after injury leads to better results such as decrease in blood loss, lower incidence of infection, shorter length of hospital stay, higher probability of graft take, and drop in mortality [34].

Early wound closure has been found to decrease severity of hypertrophic scarring, joint contractures and stiffness and promotes quicker rehabilitation [35].

In general, most areas are excised with a hand skin graft knife or powered dermatome.

In partial-thickness wounds, attempts need to be made to preserve viable dermis, whereas in full-thickness injury, all necrotic and infected tissue must be removed leaving viable wound bed of either fascia, fat, or muscle [36].

3.2 Burn Wound Coverage

Following burn wound excision, it is vital to obtain wound closure. Autografting which is the transfer of the patient's healthy skin to cover the excised burned tissue is the gold standard for burn wound coverage.

3.2.1 Skin Substitutes

With advances in burn resuscitation and critical care management, patients with large TBSA burns are surviving, leading to problems with wound coverage. This has led to the development of various biological and synthetic substrates to replace the injured skin post-burn. With the advantages of availability in large quantities, bioengineered skin substitutes, both biosynthetic and cultured autologous engineered skin, are available to provide temporary or permanent coverage [37–39].

There are different classifications of skin substitutes. The Kumar classification is the most common type. The Davison-Kotler classification is a newer type that categorizes skin substitutes based upon the following factors [39].

1. Type of biomaterials.
   (a) synthetic,
   (b) biosynthetic,
   (c) biologic,
2. Skin substitute composition regarding cellular component:
   (a) Cellular.
      - These skin substitutes consist of cells seeded within an extracellular matrix. They facilitate the release of growth factors and ECM components to enhance wound healing [40, 41].

   (b) Acellular.
      - These skin substitutes are designed to prevent fluid loss and wound bed infection. They are mainly composed of a wide range of biomaterials such as silicone, nylon mesh, acellular cadaveric dermis, and collagen [42].
3. Duration of the cover depending on its design and composition [43].
   (a) Permanent.
   (b) Semi-permanent.
   (c) Temporary.
4. Layering.
   (a) Single.
   (b) Bilayer.
5. Anatomical structure.
   (a) Epidermal.
   (b) Dermal.
   (c) Composite both epidermal and dermal components used to mimic the histological structure of normal skin [31].

Here, we will classify the skin substitutes according to anatomic structure.

3.3 Epidermal Substitutes

Act as the epidermis.

Most commonly used epidermal substitutes are cultured epithelial autografts (CEAs). These are autologous epithelial cells grown from a single full-thickness skin biopsy. These have been shown to decrease mortality in massively burned patients in a prospective, controlled trial [30]. However, widespread use of CEAs has been pri-

marily hampered by poor long-term clinical results and exorbitant costs. They have also been consistently reported to be fragile and difficult to handle even when applied on properly prepared wound beds [32, 44, 45].

There have been studies using noncultured autologous skin cell spray grafts for burns. Following application, the skin cells induce rapid epidermal regeneration achieving re-epithelialization to heal burns, donor sites, and chronic wounds. This is useful for patients having limited donor tissue availability, as well as for patients in whom the creation of donor sites may lead to significant morbidity.

Currently, commercially available autologous epidermal substitutes for clinical use include ReCell (Avita Medical Woburn, Massachusetts), Myskin (Regenerys, Cambridge, UK), (RenovaCare, Inc., NY), CellSpray (Clinical Cell Culture (C3), Perth, Australia), Epicel (Genzyme Biosurgery, Cambridge, MA, USA), EpiDex (Modex Therapeutiques, Lausanne, Switzerland), Bioseed-S (BioTissue Technologies GmbH, Freiburg, Germany), etc.

3.4 Dermal Substitutes

In contrast to cultured epidermal sheets, engineered dermal constructs can prevent wound contraction and they provide a greater mechanical stability.

To date, a wide variety of marketed dermal constructs is available. These skin substitutes can promote the healing of acute and chronic wounds by secreting extracellular matrix (ECM) proteins, a variety of growth factors and cytokines into the wound until they undergo normal apoptosis a few weeks post-implantation [46, 47].

Allografts (cadaver skin) frequently serve as skin substitute in severely burned patients. Some are chemically treated (e.g., Alloderm®), lacking the cellular elements that are responsible for the immunogenic rejection [48]. While this approach is still commonly used in burn centers throughout the world, they only provide temporary coverage. It also bears considerable risks, including antigenicity, cross-infection as well as limited availability [49].

Xenografts have been used for hundreds of years as temporary replacement for skin loss. Even though these grafts provide a biologically active dermal matrix, the immunologic disparities prevent engraftment and predetermine rejection over time [32].

Dermagraft® (Advanced Biohealing; La Jolla, CA) consists of human foreskin fibroblasts, cultured in a biodegradable polyglactin mesh [50, 51]. It stimulates ingrowth of fibrovascular tissue and epithelialization. The frozen product offers an advantage but unfortunately requires storage at −75 °C. It is thawed in sterile saline and then applied to a clean, well-debrided wound. It has a 6-month shelf life and was approved by the FDA in 2001 for full-thickness diabetic foot ulcers of more than 6 weeks' duration, extending through the dermis, but without exposed underlying structures. It has found value in healing complex surgical wounds with secondary closure.

3.5 Composite (Epidermal/Dermal) Substitutes

To date, the most advanced and sophisticated constructs that are available for clinical use. Composite skin substitutes mimic both epidermal and dermal layers of the skin. They have been shown to provide growth factors, cytokines, and ECM for host cells, thus initiating and regulating wound healing. Nevertheless, these skin substitutes are accompanied by long production time, high manufacturing cost and repeatedly fail to close the wound permanently due to tissue rejection [47].

Currently available epidermal/dermal substitutes that are in clinical use include StrataGraft (Stratatech, a Mallinckrodt Company), Epifix (MiMedx Group, Marietta, GA), MatriStem (ACell, Inc), Permaderm (Regenicis, New York, N.Y), Apligraf (Organogenesis Inc., Canton, Massachusetts, CA, USA), OrCel® (Ortec International, Inc., New York, NY, USA), PolyActive® (HC Implants BV, Leiden, The Netherlands), and TissueTech® Autograft System (Laser skin and Hyalograft 3D; Fidia Advanced Biopolymers, Abano Terme, Italy), Self-Assembled Skin Substitute (SASS) (Loex, Quebec).

These constructs are composed of autologous and allogeneic skin cells (keratinocytes and fibroblasts), which are incorporated into scaffolds.

Apligraf® was the first commercially available composite tissue analog on the market. This medical device containing living allogeneic cells was approved by the US Food and Drug Administration (FDA) in 1998 for the treatment of venous ulcers of 1 month duration that have not responded to conventional therapy. It was approved in 2000 for neuropathic diabetic ulcers of more than 3-week duration [52]. The epidermal component of this bilayer skin construct consists of neonatal foreskin keratinocytes seeded on a dermal component comprised of neonatal foreskin fibroblasts within a matrix of bovine type I collagen.

Orocel®, the first biologic cellular matrix, was initially developed in 1971 as a treatment for dystrophic epidermolysis bullosa [53].

Self-Assembled Skin Substitute (SASS) is a reconstruction of a fully autologous bilayered skin substitute without using any exogenous scaffold or biomaterial. SASS requires a 31-day production period [54, 55].

Integra® was developed in 1981 and approved by the FDA in 2002. It is a bilaminar skin equivalent composed of porous matrix of cross-linked bovine collagen and shark-derived glycosaminoglycan, attached to a semipermeable silicone layer that serves as an epidermis. The membrane helps prevent water loss and provides a flexible wound covering, while the scaffolding promotes neovascularization and new dermal growth. Cells migrate into the matrix while the bovine collagen is absorbed and replaced by the patient's dermal elements. Rebuilding of the scaffolding occurs within 2–3 weeks, at which time the silicone layer is removed, allowing re-epithelialization from the wound edge. Complete wound closure takes approximately 30 days. Indications for Integra include pressure, diabetic, chronic vascular and venous ulcers, as well as surgical wounds and has been successfully utilized in immediate and delayed closure of full-thickness burns, leading to reduction in length of hospital stay, favorable cosmetics, and improved functional outcome in a prospective and controlled clinical study [56–60]. Our group previously conducted a randomized clinical trial utilizing Integra® in the management of severe full-thickness burns of ≥50% TBSA in a pediatric patient population comparing it to standard autograft-allograft technique, and found Integra to be associated with improved resting energy expenditure and improved aesthetic outcome post-burn [61]. It has also been found to inhibit scar formation and wound contraction [62].

There are also newer skin substitutes available in the market (Table 2)

Table 2 New skin substitutes

Skin substitutes				
Type	Subtype	Name	Composition	Reference
Epidermal	Cultured epithelial autograft (CEA)	Epicel (Genzyme tissue repair Corp, Cambridge, Massachusetts)	CEA from human keratinocytes embedded in fibrin mesh. Disadvantage is the high cost, limited reliability, fragility, susceptibility to infections, complex post op care	[30, 32, 44, 45]
	Autologous skin suspension ASCS or cell spray	Recell (Avita medical Woburn, Massachusetts)	Autologous skin suspension that is produced using minimal donor skin and applied as a cell spray. Induces rapid re-epithelialization and wound healing	[83, 84]
		MySkin (Regenerys, Cambridge, UK)	Suspended CEA delivered as spray to promote re-epithelialization	[85, 86]
		Skin gun (RenovaCare, Inc., NY)	Expansion ratio of skin donor site to treatment surface area of about 1:20	[87]
		Keraheal (Seoul, Korea, MCTT)	Suspension form of cultured epithelial cells plus fibrin glue to facilitate epithelial cell attachment	[88]

(continued)

Table 2 (continued)

Skin substitutes				
Type	Subtype	Name	Composition	Reference
Dermal		Abwat (advanced wound bioengineered alternative tissue—Superficial, Aubrey Inc. Carlsbad, California)	Made of porcine collagen type I embedded in a nylon mesh and a porous silicone membrane	[89]
		OASIS wound matrix (Healthpoint ltd., Ft worth, Tex)	Derived from the submucosal layers of the porcine intestine. Contains glycosaminoglycans and growth factors	[90, 91]
		Matriderm (skin and health care AG, Billerbeck, Germany)	Made of type I collagen fiber coated with 3% a-elastin hydrosylate matrix. Can be used as one-stage procedure with STSG.	[92]
		Biodegradable temporizing matrix, BTM (PolyNovo, Melbourne, Australia)	Composed of biodegradable polyurethrane foam plus a temporary nonbiodegradable polyurethrane seal. Fully synthetic, making it cheaper to produce	[93]
		Matristem (Acell, Inc., Columbia, MD, USA)	Composed of extracellular matrix derived from porcine urothelium. Provides barrier protection	[94]
		Integra (LifeSciences, Plainsboro, NJ, United States)	Bovine collagen matrix with a silicone layer. Most studied dermal replacement matrix	[10, 14]
		Alloderm (LifeCell, Branchburg, N.J.)	Human cadaveric acellular matrix	[48, 49]
		Suprathel (Polymedics, Atlanta GA)	Synthetic copolymer >70% DL-lactide polymerized with ε-caprolactone and methylenecarbonate	[93]
Composite		Permaderm (Regenicis, New York, N.Y)	Autologous fibroblasts and keratinocytes embedded with collagen and glycosaminoglycan substrates	[95]
		Self-assembled skin substitute (SASS) (Loex, Quebec)	Reconstruction of a fully autologous bilayered skin substitute without using any exogenous scaffold or biomaterial. Requires a 31-day production period [28, 29].	[54, 55]
		Epifix (MiMedx group, Marietta, GA)	Composed of dehydrated amniotic and chorionic membrane containing collagen, connective tissue, cytokines, and growth factors	[96]
		SkinTE (PolarityTE, Salt Lake City, UT)	An autologous homologous skin construct derived from full-thickness skin	[97]
		Cultured skin substitute (Cincinnati, USA)	Autologous keratinocytes and fibroblasts from patient biopsy, combined into a bilayer with bovine collagen matrix	[98]

4 Adjuncts

To further stimulate healing, several adjuvant treatment methods have been developed.

4.1 Negative Pressure Wound Therapy (NPWT)

NPWT is a wound dressing system than continuously or intermittently applies subatmospheric pressure to the surface of the wound. NPWT has been commonly used in various acute and chronic wounds [63, 64]. Majority of published literature on the use of NPWT for burns is on the use of NPWT used in skin grafting to bolster the grafts which helps promote the growth of granulation tissue → increasing the success rate of graft take. There are a few studies *on the use of NPWT on acute burn and* there is promising evidence to suggest NPWT may reduce edema and wound progression [65–67].

NPWT promotes healing through exudate removal, increase in tissue perfusion, and by exerting tensile forces on the local tissue environment; they create cellular deformation that results in mitotic activity and cell proliferation [68, 69]. NPWT is contraindicated on wounds with exposed vessels, malignancy, necrotic tissue, and untreated osteomyelitis [70, 71].

4.2 Hyperbaric Oxygen (HBOT)

HBOT is a treatment modality that has been used as an adjunct in wound healing for over 40 years. The patient undergoes multiple treatments lasting for 60–120 min inside a sealed chamber with 100% pressurized oxygen at 1.5–3 atmospheres absolute (ATA) [72].

Recent studies have shown that HBOT is safe and effective for improving burn wound healing by improving tissue oxygen and phagocytosis, preventing dermal ischemia, reducing edema, modulating the zone of stasis, preventing partial- to full-thickness conversion, and preserving cellular metabolism [73–75]. HBOT has been demonstrated to be safe and effective. However, more data are needed before broad conclusions can be made about the overall utility of hyperbaric oxygen for treating burns [76, 77].

5 What's Next?

There are multiple ongoing clinical trials on the use of new skin substitutes in the treatment of burn injuries. One of the interesting focus of bioengineering and regenerative science is on the use of stem cells and the development of the 3D skin printer.

5.1 Stem Cells

The influence of stem cells on wound healing is very promising. Mesenchymal stem cells (MSCs) enhance wound healing through differentiation and angiogenesis. They also regulate the immune response and inflammation [78]. Preclinical and clinical trials show that MSC therapy accelerates wound closure [79].

5.2 3D Skin Printing

A solid 3D structure is made through a 3D printer by sequentially delivering thin layers of materials and bonding them together [80]. For 3D skin printing, this involves delivery of cells layer by layer, along with scaffolding materials using a microfluidic cartridge over the burned area. The use of 3D bioprinting is quite promising. However, there are still a lot of technological and regulatory challenges that need to be overcome [81, 82].

6 Summary

Loss of the normal skin barrier function causes the common complications of burn injury. These include infection, loss of body heat, increased evaporative water loss, and change in key interactive functions such as touch and appearance. Excessive scar formation in the areas of a deep dermal burn represents an additional well-known side effect that significantly affect the patient's quality of life, both physically and psychologically.

Early excision and early closure of the burn wound has been probably the single greatest advancement in the treating patients with severe thermal injuries during the last 20 years. Despite all efforts, an off-the-shelf, full-thickness skin replacement is not yet available. A future prospective is to incorporate cellular growth-enhancing substances or additional cell types, besides keratinocytes and fibroblasts, in the bioengineered skin substitutes to obtain constructs with improved function and higher resemblance to native skin. The development of gene transfer technology and the use of stem cells appear to be a promising means in this context.

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Nutrition of the Burned Patient and Treatment of the Hypermetabolic Response

Marc G. Jeschke

1 Introduction

Advances in therapy strategies, based on improved understanding of resuscitation, enhanced wound coverage, more appropriate infection control and improved treatment of inhalation injury improved the clinical outcome of burn patients over the past years [1, 2]. However, severe burns remain a devastating injury affecting nearly every organ system and leading to significant morbidity and mortality [2]. One of the main contributors to adverse outcome of this patient population is the profound stress-induced hypermetabolic response, associated with severe alteration in glucose, lipid, and amino acid metabolism (Fig. 1) [1, 3–5].

2 Post-Burn Hypermetabolism

A hallmark for severely burned patients is the hypermetabolic response that is not only very profound but also extremely complex and most likely induced by stress and inflammation [1, 3–5]. The cause of this response is not entirely defined, but it has been suggested that sustained increases in catecholamine, glucocorticoid, glucagon, and dopamine secretion are involved in initiating the cascade of events leading to the acute hypermetabolic response with its ensuing catabolic state [6–15]. In addition, cytokines, endotoxin, neutrophil-adherence complexes, reactive oxygen species, nitric oxide, and coagulation as well as complement cascades have also been implicated in regulating this response to burn injury [16]. Once these cascades are initiated, their mediators and by-products appear to stimulate the persistent and increased metabolic rate associated with altered glucose, lipid, and amino acid metabolism seen after severe burn injury [17].

The metabolic changes post-burn occur in two distinct pattern of metabolic regulation following injury [18]:

1. *The first phase occurs within the first 48 h of injury and has classically been called the "ebb phase"* [18, 19], characterized by decreases in cardiac output, oxygen consumption, and metabolic rate as well as impaired glucose tolerance associated with its hyperglycemic state.
2. The lower metabolic response then gradually increase within the *first 5 days post-injury to a plateau phase: flow phase*; characteristically associated with hyperdynamic circulation and the above-mentioned hypermetabolic state. Insulin release during this time period was

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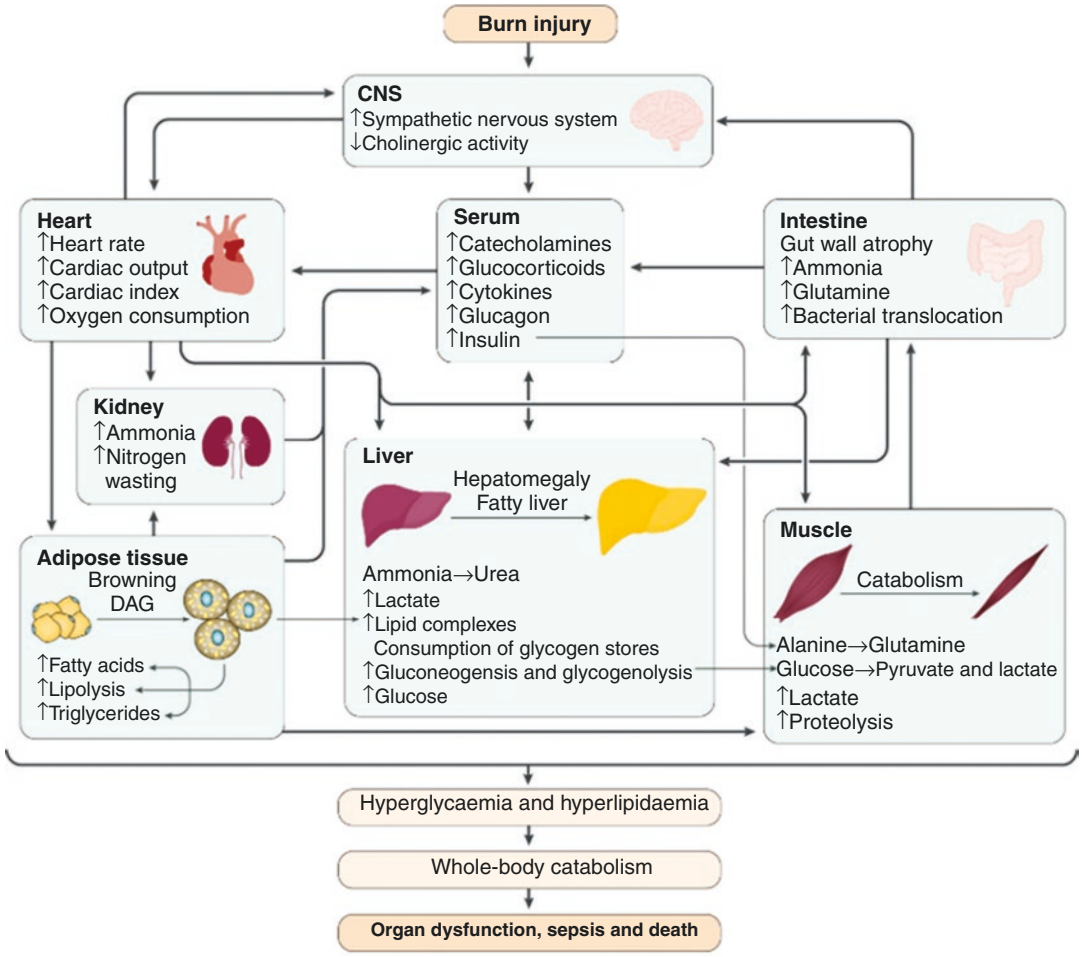

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Fig. 1 Hypermetabolic state in burn injury. Severe burn injury induces a unique and remarkably complex response that involves the release of stress hormones and pro-inflammatory mediators. The immediate response leads to a hypometabolic response that lasts for ~72–96 h (Ebb phase), but then rapidly turns into the flow phase that can persist for years after the initial injury. Stress mediators, such as catecholamines, glucocorticoids, and cytokines, are released into the system and cause a plethora of systemic responses. The heart goes into a hyperdynamic overdrive, increasing circulation and blow flow to increase oxygen and nutrient delivery. However, increased stress signaling causes changes in organ function and metabolic demand. Protein is degraded to deliver energy for hepatic function; the gut develops mucosal atrophy to absorb more nutrients but also enables bacterial translocation. The kidneys are hyperperfused but oxygen delivery decreased, leading to acute kidney injury and stress signals from the kidney. The interplay between these organs accumulate, leading to conversion to this metabolic and inflammatory overdrive subsequently causing white adipose tissue change to brown adipose tissue. Brown adipose tissue releases energy and induces substantial lipolysis and with accompanying appearance of lipotoxic intermediates, such as triglycerides, free fatty acids, and diacylglycerols (DAG), all of which are transferred to the liver. The liver is unable to metabolize all of the accumulating substances and develops hepatomegaly. In turn, hyperlipidemia and hyperglycemia with insulin resistance is present, which worsens the hypermetabolic and inflammatory state. If hypermetabolism cannot be diminished or decreased, this response leads to holistic catabolism and, subsequently, to multiple organ failure and death

found to be twice that of controls in response to glucose load [20, 21] and plasma glucose levels are markedly elevated, indicating the development of an insulin resistance [22, 23]. In addition, lipolysis is tremendously increased leading to increased free fatty acids and triglycerides. Current understanding has been that these metabolic alterations resolve soon after complete wound closure. However, recent studies found that the hypermetabolic response to burn injury lasts significantly longer; we found in recent studies that sustained hypermetabolic alterations post-burn, indicated by persistent elevations of total urine cortisol levels, serum cytokines, catecholamines, and basal energy requirements, were accompanied by impaired glucose metabolism and insulin sensitivity that persisted for up to 3 years after the initial burn injury [24]. These results indicate the importance of long-term follow-up and treatment of severely burned patients.

Post-burn hypermetabolism is initiated to provide sufficient energy for maintaining organ function and whole-body homeostasis under demanding trauma conditions [25–28]. Unfortunately, prolonged hypermetabolism becomes detrimental and is associated with vast catabolism, multi-organ failure, and death [1, 29, 30]. Various studies have found that the metabolic need of a burn patient is the highest of any medical state, approaching 140% of that predicted. The hypermetabolic response involves a vast number of pathways but there are two, in particular, that appear to most profoundly affect post-burn outcomes: glucose metabolism with insulin resistance (IR) and hyperglycemia [31–34], as well as lipid metabolism with increased lipolysis [35–38].

2.1 Glucose Metabolism

During the early post-burn phase, hyperglycemia occurs as a result of an increased rate of glucose appearance, along with an impaired tissue extraction of glucose, leading to an overall increase of glucose and lactate [28, 39]. Of major importance is recent evidence strongly suggesting that hyperglycemia is detrimental and associated with adverse clinical outcomes in severely burned patients. Specifically, studies in burn patients indicated that hyperglycemia is associated with increased infections and sepsis, increased incidence of pneumonia, significantly increased catabolism and hypermetabolism, and, most importantly, with increased post-burn mortality [31–34, 40, 41]. The evidence that hyperglycemia is detrimental in burn patients was further supported by a prospective randomized trial that showed that glucose control is beneficial in terms of post-burn morbidity and organ function [34]. Retrospective cohort studies further confirmed a survival benefit of glucose control in severely burned patients [33, 41]. These data strongly indicate that IR and hyperglycemia represent a significant clinical problem in burn patients and are clearly associated with poor outcome.

Although the dire consequences of burn-induced hyperglycemia have been delineated, the molecular mechanisms underlying IR, and hyperglycemia are not entirely defined. Accordingly, ER stress was recently identified as one of the central intracellular stress signaling pathways linking IR, hyperglycemia, and inflammation [42]. Since inflammation, IR, and hyperglycemia are central characteristics of the post-burn response [3], we investigated in a preliminary study whether a severe burn induces ER stress and the unfolded protein response (UPR) in severely burned patients. As expected, we found that a severe thermal injury induces ER stress in the metabolically active tissues skin, fat, and muscle [43]. We therefore have evidence suggesting that ER stress may be central to orchestrating and inducing inflammatory and hypermetabolic responses post-burn on a cellular level.

2.2 Fat Metabolism

The other metabolic pathway that is significantly altered during the post-burn hypermetabolic response is lipid metabolism, which may be related to changes in insulin resistance. Lipolysis consists of the breakdown (hydrolysis) of triacylglycerol into free fatty acids (FFA) and glycerol.

Notably, lipolysis, and free fatty acids not only contribute to post-burn morbidity and mortality by fatty infiltration of various organs, but it was also shown that FFAs can mediate insulin resistance [44]. Specifically, FFAs impair insulin-stimulated glucose uptake [45, 46] and induce insulin resistance through inhibition of glucose transport activity [47]. In the context of type 2 diabetes, it has been shown that increased FFA levels are predictive for incidence and severity of the disease [48]. One of the major alterations post-burn is significantly increased lipolysis, and several studies have suggested that increased lipolysis can be attributed to increased catecholamine levels [49, 50]. Interestingly, despite increased lipolysis, plasma FFA concentrations can be increased or decreased which can be due to hypo-albuminemia or increased intracellular FFA turnover, which is part of the futile cycle involving the breakdown of adipose and muscle TGs into FFA. Regardless, increased triglycerides and FFA lead to fatty infiltration of vital organs, especially the liver. Accordingly, fatty liver is very common post-burn and is associated with increased clinical morbidities, as well as metabolic alterations. Post-burn pathology examinations [51, 52] and spectroscopy studies have shown that burned children have a 3- to 5-fold increase in hepatic triglycerides [53, 54], associated with increased incidence of infection, sepsis, and poor outcome [38]. In addition, hepatic triglyceride levels were higher than those found in diabetic elderly patients, underscoring the metabolic link between fatty infiltration and insulin resistance. This data is in agreement with various other recent studies that showed a strong relationship between fat and glucose metabolism [55]. Though this relationship is clear, the mechanism by which lipids induce insulin resistance is not entirely defined.

Even more important is, that recently, adipose tissue has been recognized as an essential player in the induction and persistence of hypermetabolism after burn injury. Like cold stress, burn injury induces the browning of white adipose tissue (WAT), in which subcutaneous WAT converts to a more brown-like adipose termed beige/brite adipose tissue (BAT) [56, 57]. These otherwise quiescent beige cells adopt brown-like features, including multilocular lipid droplets and high UCP1 expression. Moreover, browning drives a conversion in mitochondrial function, uncoupling the respiratory chain from ATP synthesis and predominantly producing heat, thereby sending these already hypermetabolic patients into metabolic overdrive. While browning can have beneficial effects in patients with obesity and diabetes, others and we believe that browning in burn patients fuels high metabolic rates and alters plasma lipid profiles, leading to accelerated development and progression of cachexia, hyperglycemia, and organ steatosis thereby worsening outcome of severely burned patients. Although the physiology of browning has been demonstrated, the exact function and mechanisms are essentially unknown in burn injury. However, this exciting new field will lead to some novel insights and developments that will hopefully result in attenuation of the hypermetabolic response.

2.3 Protein Metabolism

Protein/amino acids from skeletal muscle is the major source of fuel in the burned patient, which leads to marked wasting of lean body mass (LBM) within days after injury [1, 58]. Since skeletal muscle has been shown to be responsible for 70–80% of whole-body insulin-stimulated glucose uptake, decreases in muscle mass may significantly contribute to this persistent insulin resistance post-burn [59]. A 10–15% loss in lean body mass has been shown to be associated with significant increases in infection rate and marked delays in wound healing. The resultant muscle weakness was further shown to prolong mechanical ventilatory requirements, inhibit sufficient cough reflexes, and delay mobilization in protein-malnourished patients, thus markedly contributing to the incidence of mortality in these patients [60]. Persistent protein catabolism may also account for delay in growth frequently observed in our pediatric patient population for up to 2 years post-burn [4].

Various groups suggest that hypermetabolism is a major contributor to poor outcome post-burn

and that treatment or alleviation of the hypermetabolic response is beneficial for patient outcomes.

3 Attenuation of the Hypermetabolic Response

3.1 Nonpharmacologic Strategies

3.1.1 Nutrition

The primary goal of nutritional support is to provide an adequate energy supply and the nutrients necessary to maintain organ function and survival. Early adequate enteral nutrition alleviates catabolism and improves outcomes [61]. However, overfeeding, in form of excess calories and/or protein is associated with hyperglycemia, carbon dioxide retention, fatty infiltration of organs, and azotemia [58]. Therefore, nutrition is an essential component to alleviate hypermetabolism, but too much feeding is detrimental and should not be pursued.

Nutritional Route

The preferred route to administer nutrition is oral/NG or NJ tubers. Enteral nutrition (EN) decreases bacteremia, reduces sepsis, maintains motility of the gut, and preserve "first pass" nutrient supply to the liver [61]. In cases where enteral feeding is not applicable (e.g., prolonged ileus or intolerance to enteral feeding), parenteral nutrition should be used to maintain appropriate macro- and micronutrient intake. Parenteral nutrition remains of critical importance in burn patients in whom appropriate dietary support cannot be achieved or in those whose total caloric requirements cannot be fully supplied via enteral nutrition alone.

Initiation of Nutrition

Recently, the initiation of adequate nutrition-gained attention and several studies delineated that optimal nutritional support for severely burned patient is best accomplished by early (within 12 h after injury) initiation [62]. Beside clinical data, there are animal studies showing that early initiation of enteral nutrition can significantly attenuate the post-burn hypermetabolic responses to severe burn outlined above [61]. Patients with severe burn injury can be safely enterally fed in the duodenum or jejunum within 6 h post-burn, whether or not they have total gastro-duodenal function [63]. Thus, nasojejunal or nasoduodenal feeding should be administered early.

Amount of Nutrition

As aforementioned under—as well as overfeeding is associated with adverse outcomes. Currently, resting energy requirements of burned patients are commonly estimated using equations that incorporate body mass, age, and gender. The performance of these equations has been compared to actual measured resting energy expenditure, which is obtained through indirect calorimetry.

Validation and agreement analysis of formulas such as the Harris-Benedict, Schofield HW, Curreri, and World Health Organization formulas have shown that, although these formulas are based on patient-specific factors such as age, gender, weight, and burn size, they may significantly overestimate caloric requirements in burn patients, increasing the risk of overfeeding and its subsequent deleterious effects [64, 65]. Recently, the adapted Toronto equation seem to be a better formula to calculate REE, as the calculated results very closely matched the MREEs.

We therefore recommend to measure resting energy expenditure via indirect calometry and adjust nutrition to this estimation. A factor of 1.2–1.4 is applied to the results of these formulas accounting for the burn hypermetabolic response.

Composition of Nutrition

At the moment, no ideal nutrition for burn patients exists. There are only recommendations and we at RTBC recommend the use of a high glucose, high protein/amino acid, low-fat nutrition with some unsaturated fatty acids.

We believe that the major energy source for burn patients should be carbohydrates and amino acids thereby sparing protein from oxidation for energy, allowing the protein to be effectively

used by the skin and organs. It is estimated that critically ill, burned patients have caloric requirements that far exceed the body's ability to assimilate glucose, which has been reported to be 5 mg/kg/min or approximately 7 g/kg/day (2240 kcal for an 80 kg man) [66, 67]. However, providing a limited amount of dietary fat diminishes the need for carbohydrates and ameliorates glucose tolerance.

Although the hypermetabolic response to severe burns stimulates lipolysis, the extent to which lipids can be utilized for energy is limited. Thus, fat should comprise less than 25% of non-protein calories [68]. Recently, several studies were conducted on the composition of administered fat which showed that the composition of fat is more important than the quantity. Most common lipid sources contain omega-6 polyunsaturated fatty acids such as linoleic acid, which are metabolized to arachidonic acid, a precursor of pro-inflammatory molecules such as prostaglandin E2 2,66. Omega-3 fatty acids are metabolized without producing pro-inflammatory compounds. Diets high in omega-3 fatty acids have been associated with an improved inflammatory response, improved outcomes, and reduced incidences of hyperglycemia [69].

Proteolysis is another hallmark of the hypermetabolic response after severe burn injury and protein loss can exceed 150 g/day [58]. Increased protein catabolism leads to compromised organ function, decreased wound healing, immunoincompetence, and loss of LBM [58]. Evidence suggests that providing a larger protein replacement pool is helpful after severe burn injury. [70, 71] While research has shown that healthy individuals require approximately 1 g/kg/day of protein intake [27, 72–74], in vivo kinetic studies on oxidation rates of amino acids have shown that utilization rates in burned patients are at least 50% higher than those in healthy, fasting individuals [70, 71]. Thus, at least 1.5–2.0 g/kg/day protein should be given to burn patients. However, supplementation with higher amounts protein needs to be evaluated carefully as they may fail to yield improvements in muscle protein synthesis or LBM and may serve only to elevate urea production.

Amino acids supplementation was and is controversially discussed, especially alanine and glutamine. Both are important transport amino acids to supply energy to the liver and skin to increase healing mechanisms and metabolic needs [27, 75, 76].

Table 1 showed an overview of various feeds and composition thereof.

Table 1 Dietary reference intakes (DRIs): vitamin and trace elements requirements[a]

Age	Vit A (IU)	Vit D (IU)	Vit E (IU)	Vit C (mg)	Vit K (mcg)	Folate (mcg)	Cu (mg)	Fe (mg)	Se (mcg)	Zn (mg)
0–13 years										
Non-burned	1300–2000	200	6–16	15–50	2–60	65–300	0.2–0.7	0.3–8	15–40	2–8
Burned	2500–5000			250–500		1000[b]	0.8–2.8		60–140	12.5–25
≥13 years (includes adults)										
Non-burned	2000–3000	200–600	23	75–90	75–120	300–400	0.9	8–18	40–60	8–11
Burned	10,000			1000		1000[b]	4.0		300–500	25–40

RDI Reference Daily Intake refers to the daily intake level that a healthy person should achieve. Conversion based on: 1 mcg of Vit A = 3.33 IU of Vit A; 1mcg of calciferol = 40 IU of Vit D; 1 mg of α-tocopherol = 1.5 IU of Vit E

[a]SOURCES: Dietary Reference Intakes for Calcium, Phosphorous, Magnesium, Vitamin D, and Fluoride (1977); Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline (1988); Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids (2000); and Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc (2001). These reports may be accessed at http://www.nap.edu

[b]Administered Monday, Wednesday, and Friday

Glutamine also serves as a primary fuel for enterocytes and lymphocytes maintaining small bowel integrity, preserving gut-associated immune function, and limiting intestinal permeability following acute injury [77, 78]. Glutamine is quickly depleted post-burn from serum and muscle [77, 78]; however, this depletion mainly occurs intracellularly, and it is very difficult to deliver Glutamine effectively to the cells. Small studies in burn patients indicated that Glutamine supplementation decreased incidence of infection, length of stay and mortality [77, 78]. Therefore, there is a signal that Glutamine supplemental maybe associated with beneficial effects. A current multicenter trial (REDOX) is addressing the answer and the results are expected over the next 4–5 years. The literature on *Alanine* is even sparser, and at this time there is no evidence to administer or not administer Alanine. Furthermore, there are no signal whether or not to supplement branched-chain amino acids which improve nitrogen balance [79].

Another important component affected by burns are *vitamins, micronutrients, and trace elements* [80]. Decreased levels of Vitamins A, C, D, E, iron, copper, zinc, and selenium have been implicated in wound healing deficiencies and immune dysfunction after severe burn injury [80, 81]. Vitamin A replacement is particularly important for wound healing and epithelial growth. Vitamin C is paramount for the synthesis and cross-linking of collagen post-burn, and burn patients often require up to 20 times the recommended daily allowance [81, 82]. Vitamin D levels are low in burned children, and adequate Vitamin D status is likely essential for attenuating further loss of bone minerals post-burn [81, 82]. Trace elements, primarily iron, zinc, selenium, and copper, are required for humoral and cellular immunity [83–89]. Iron is also an important cofactor in oxygen-carrying proteins [58]. Zinc supplementation aids in wound healing, DNA replication, lymphocyte function, and protein synthesis [83–89]. Selenium replacement improves cell-mediated immunity and activates the transcription factor NFkB, a significant modulator of the inflammatory response [83–89]. Copper is critical for collagen synthesis and wound healing [84]. Deficiencies in copper, in particular, have been linked to fatal arrhythmias and poor outcomes [83–89]. Plasma levels of these trace elements are significantly depressed for prolonged periods after the acute burn injury due to increased urinary excretion and significant cutaneous losses. Replacement of these micronutrients lessens morbidity in severely burned patients [83–89]. Therefore, a complete daily multi-vitamin/mineral supplementation should be given (Table 2).

3.1.2 Early Excision

Early excision and closure of the burn wound has been probably the single greatest advancement in the treating patients with severe thermal injuries during the last two decades leading to substantially reduced resting energy requirements, subsequent improvement of mortality rates and substantially lower costs in this particular patient population [1, 90, 91]. It is in our opinion imperative to excise the burn wounds early and cover the excised areas with temporary cover materials or autologous skin. This will decrease the burn-induced inflammatory and stress responses leading to decreased hypermetabolism.

3.1.3 Environmental Support

Burn patients can lose as much as 4000 mL/m^2 burned/day of body water through evaporative loss from extensive burn wounds that have not definitive healed [92]. The altered physiologic state resulting from the hypermetabolic response attempts to at least partly generate sufficient energy to offset heat losses associated with this inevitable water loss. The body attempts to raise skin and core temperatures to 2 °C greater than normal. Raising the ambient temperature from 25 to 33 °C can diminish the magnitude of this obligatory response from 2.0 to 1.4 resting energy expenditure in patients exceeding 40% TBSA. This simple environmental modulation, meaning raise room temperature is an important primary treatment goal that frequently is not realized [93].

Table 2 Selected enteral nutrition options for burned patients—US Market

Nutrition	kcal/mL	CHO g/L (% Cal)	PRO g/L (% Cal)	Fat g/L (% Cal)	Comments
Pediatric					
Vivonex RTF	1	175 (70%)	50 (20%)	12 (**10%**)	Transitional feeding, low fat, high CHO, easily digestible
Vivonex TEN	1	210 (82%)	38 (15%)	2.8 (**3%**)	Free AA, very low fat, high CHO [137] severe trauma or surgery
Impact glutamine	1.3	150 (46%)	78 (24%)	43 (30%)	Immunonutrition, GLN, ARG, omega-3 fatty acids
Elecare	0.67	72 (43%)	20 (15%)	32 (42%)	Prepared at 9.4 g/60 mL, AA-based nutrition
Adult					
Crucial	1.5	89 (36%)	63 (25%)	45 (39%)	Immune-enhancing with ARG concentrated
Impact	1.0	130 (53%)	56 (22%)	28 (**25%**)	Immune-enhancing with ARG, GLN, fiber
Oxepa	1.5	105 (28%)	63 (17%)	94 (55%)	ALI, ARDS period (2 weeks) [138] concentrated
Glucerna	1.0	96 (34%)	42 (17%)	54 (49%)	For glucose intolerant or diabetic patients, low CHO
Nepro	1.8	167 (34%)	81 (18%)	96 (48%)	For CKD and patients on dialysis concentrated
Osmolite 1 Cal	1.06	144 (54%)	44 (17%)	35 (**29%**)	Isotonic, for use in intolerance to hyperosmolar nutrition
Modular (children/adult)					
Benefiber powder	0.27	66 (100%)			(prepared at 4 g/60 mL) tasteless, odorless, soluble fiber
Beneprotein	0.83		200 (100%)		(prepared at 7 g/30 mL) whey protein, mixed in foods

Data extrapolated from "Enteral product Reference Guide, by Nestle Clinical Nutrition 2010" Minneapolis, MN; and "Abbott Nutrition Pocket Guide © 2010"

CHO Carbohydrate, *PRO* protein, *AA* Amino Acid, *GLN* Glutamine, *ARG* Arginine, *ALI* Acute Lung Injury, *ARDS* Acute Respiratory Distress Syndrome, *CKD* Chronic Kidney Disease

3.1.4 Exercise and Adjunctive Measures

A balanced physical therapy program is a crucial yet easy intervention to restore metabolic variables and prevent burn-wound contracture. Progressive resistance exercises in convalescent burn patients can maintain and improve body mass, augment incorporation of amino acids into muscle proteins, and increase muscle strength and endurance [64, 94]. It has been demonstrated that resistance exercising can be safely accomplished in pediatric burn patients without exercise-related hyperpyrexia as the result of an inability to dissipate the generated heat (Fig. 2) [64, 94].

3.2 Pharmacologic Modalities

3.2.1 Recombinant Human Growth Hormone

Daily intramuscular administration of recombinant human growth hormone (rhGH) at doses of 0.1–0.2 mg/kg as a daily injection during acute burn care has alleviated inflammatory and stress responses [95, 96], increased insulin-like growth factor-I (IGF-I) [97], increased muscle protein kinetics and maintained muscular growth [98, 99], decreased donor site healing time and quality of wound healing [90], improved resting energy expenditure and decreased cardiac output [100]. However, in a prospective, multicenter,

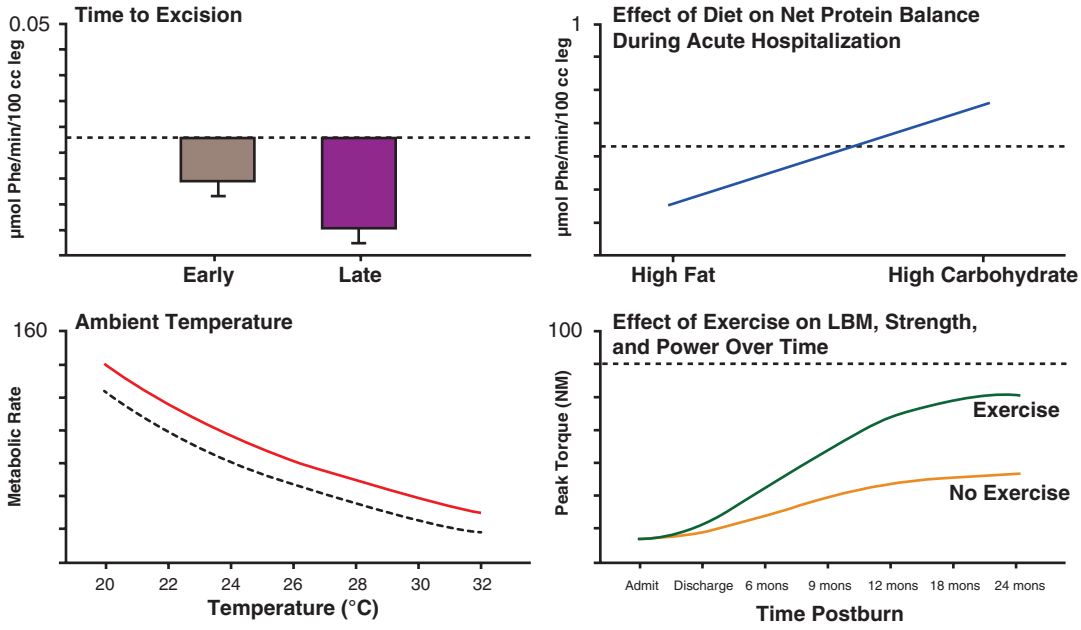

Fig. 2 Nonpharmacologic modulations of the hypermetabolic response post-burn. Demonstrates effect of early excision and grafting, environmental thermoregulation, high-carbohydrate diet and exercise on physiologic derangements post-burn.[105] Graphs are averages ± SEM. White bars represent patients with burns ≥40% total body surface area (TBSA) that had early excision. Striped bars represent patients with burns ≥40% TBSA that had late excision of burn eschar. Averages for burn patients are represented by solid curves. Values from non-burned, normal patients are represented by dashed lines (—). (Adapted from Williams FN et al. JACS 2009 Apr, 208(4): 489–502)

double-blind, randomized, placebo-controlled trial involving 247 patients and 285 critically ill non-burned patients Takala and others found that high doses of rhGH (0.10 ± 0.02 mg/kg BW) were associated with increased morbidity and mortality [101]. Others demonstrated growth hormone treatment to be associated with hyperglycemia and insulin resistance [102, 103]. However, neither short- nor long-term administration of rhGH was associated with an increase in mortality in severely burned children [9, 104].

3.2.2 Insulin-Like Growth Factor

Because IGF-I mediates the effects of GH, the infusion of equimolar doses of recombinant human IGF-1 and IGFBP-3 as a complex called IGF-I/BP-3 to burned patients improved protein metabolism in catabolic pediatric subjects and adults with significantly less hypoglycemia than rhGH itself [105]. IGF-I/BP-3 attenuates muscle catabolism and improves gut mucosal integrity, improves immune function, attenuate acute phase responses, increased serum concentrations of constitutive proteins, and decreased inflammatory responses [105–108]. However, unpublished data showed that the complex of IGF-I/Bp-3 increased neuropathies in severely burned patients and is therefore on hold for clinical use at this moment. Various studies by other investigators indicate the use of IGF-1 alone is not effective in critically ill patients without burns.

3.2.3 Oxandrolone

Treatment with anabolic agents such as oxandrolone, a testosterone analog which possesses only 5% of its virilizing androgenic effects, improves muscle protein catabolism via an increase in protein synthesis [109], reduces weight loss, and increases donor site wound healing [68]. In a prospective randomized study, Wolf and colleagues demonstrated that administration of 10 mg of oxandrolone BiD decreased hospital stay and

affected morbidity and mortality [110]. In a large prospective, double-blinded, randomized single-center study, oxandrolone given at a dose of 0.1 mg/kg BiD shortened length of acute hospital stay, maintained LBM, and improved body composition and hepatic protein synthesis [111]. The effects were independent of age [112, 113]. Long-term treatment with oxandrolone decreased elevated hypermetabolism, and significantly increased body mass over time, lean body mass at 6, 9, and 12 months after burn, and bone mineral content by 12 months after injury vs unburned controls [114, 115]. Patients treated with oxandrolone show few complications, but it should be noted that oxandrolone can increase hepatic enzymes indicating liver damage, especially during acute hospitalization. We recommend checking liver enzymes and markers regularly and in case of hepatic enzyme elevation to stop oxandrolone immediately. In addition, there are reports of oxandrolone causing increased pulmonary fibrosis. If there is any suspicion of pulmonary problems, oxandrolone needs to be stopped.

The dose for adults is 0.1 mg/kg BiD, elderly 0.05 mg/kg BiD.

3.2.4 Propranolol

Beta-adrenergic blockade with propranolol represents probably the most efficacious anti-catabolic therapy in the treatment of burns. Acute administration of propranolol exerts anti-inflammatory and anti-stress effects. Propranolol reduces skeletal muscle wasting and increases lean body mass post-burn [116, 117] and improves glucose metabolism by reducing insulin resistance. Long-term use of propranolol during acute care in burn patients, at a dose titrated to reduce heart rate by 15–20%, was noted to diminish cardiac work [118]. It also reduced fatty infiltration of the liver, which typically occurs in these patients as the result of enhanced peripheral lipolysis and altered substrate handling. Reduction of hepatic fat results from decreased peripheral lipolysis and reduced palmitate delivery and uptake by the liver [38, 119].

The dose for children is 4 mg/kg/q24 given q6 h.

The dose for adults is 10 mg TiD and increased if needed to decrease heart rate to <100 BpM.

3.2.5 Insulin

Insulin is a fascinating hormone because of its multifactorial effects. Besides its ability to alter glucose metabolism, insulin has effects on fat and amino acid metabolism and is anabolic.

Stress-induced diabetes with hyperglycemia and insulin resistance during acute hospitalization is a hallmark of severely burned patients, and a common pathophysiological phenomenon [3]. During the early phases of post-burn, hyperglycemia occurs as a result of an increased rate of glucose appearance along with an impaired tissue extraction of glucose, leading to an increase of glucose and lactate [28, 39]. This pathophysiological post-burn response is similar to the pathophysiology of type 2 diabetes, differing only in its acute onset and severity. Stress-induced hyperglycemia is associated with adverse clinical outcomes after severe burn [31, 32]. Burned patients with poor glucose control have a significantly higher incidence of bacteremia/fungemia and mortality compared to burn patients who have adequate glucose control [31, 32]. We also found that hyperglycemia exaggerates protein degradation, enhancing the catabolic response [31, 32]. Stress-induced diabetes with its insulin resistance and hyperglycemia can be overcome by exogenous insulin administration, which normalizes glucose levels and improves muscle protein synthesis, accelerates donor site healing time, and attenuates lean body mass loss and the acute phase response [12, 120–126]. These data indicate that hyperglycemia associated with insulin resistance represents a significant clinical problem in burn patients and that insulin administration improves morbidity and mortality.

Intensive insulin administration in severely burned patients is associated with beneficial clinical outcomes [12, 41, 120–126]. Intensive insulin therapy to maintain tight euglycemic control, however, represents a difficult clinical effort which has been associated with hypoglycemic episodes. Therefore, the use of a continuous hyperinsulinemic, euglycemic clamp throughout ICU stay has been questioned in multiple multicenter trials throughout the world and has resulted in a dramatic increase in serious hypoglycemic episodes [127]. In a recent multicenter trial in

Europe (Efficacy of Volume Substitution and Insulin Therapy in Severe Sepsis (VISEP)), the effect of insulin administration on morbidity and mortality in patients with severe infections and sepsis was investigated [128]. The authors found that insulin administration did not affect mortality but the rate of severe hypoglycemia was fourfold higher in the intensive therapy group when compared to the conventional therapy group [128]. Maintaining a continuous hyperinsulinemic, euglycemic clamp in burn patients is particularly difficult because these patients are being continuously fed large caloric loads through enteral feeding tubes in an attempt to maintain euglycemia. As burn patients require weekly operations and daily dressing changes, the enteral nutrition occasionally has to be stopped, which leads to disruption of gastrointestinal motility and the risk of hypoglycemia.

We conducted a study to determine the ideal glucose target in severely burned children. We found that 130 mg/dL is the best glucose target because of glucose levels below 150–160 mg/dL but avoiding detrimental hypoglycemia. Therefore, we recommend at the current time to implement glucose control to a target of 1300 mg/dL using insulin.

3.2.6 Metformin

Metformin (Glucophage), a biguanide, has recently been suggested as an alternative means to correct hyperglycemia in severely injured patients [129]. By inhibiting gluconeogenesis and augmenting peripheral insulin sensitivity, metformin directly counters the two main metabolic processes which underlie injury-induced hyperglycemia [130, 131]. In addition, metformin has been rarely associated with hypoglycemic events, thus possibly eliminating this concern associated with the use of exogenous insulin [130, 132–134]. In a small randomized study reported by Gore and colleagues, metformin reduced plasma glucose concentration, decreased endogenous glucose production, and accelerated glucose clearance in severely burned [129]. A follow-up study looking at the effects of metformin on muscle protein synthesis confirmed these observations and demonstrated an increased fractional synthetic rate of muscle protein and improvement in net muscle protein balance in metformin-treated patients [130]. A recent clinical trial by Jeschke et al. looked at the use of Metformin and its efficacy in terms of glucose modulation without causing hypoglycemia. The authors showed that Metformin decreased glucose levels that were non-inferior to insulin levels; more importantly, however, was the finding that Metformin is superior in terms of hypoglycemia. While insulin caused an incidence of 15% hypoglycemic episodes, Metformin only caused 2% hypoglycemia indicating superiority compared to insulin [135]. Of importance is to note that the authors did not observe any incidence of lactic acidosis. Metformin is known to cause or be associated with lactic acidosis [136]. The authors propose to avoid metformin-associated lactic acidosis; the use of this medication is contraindicated in certain diseases or illnesses in which there is a potential for impaired lactate elimination (hepatic or renal failure) or tissue hypoxia. Currently, metformin should not be given if eGFR is <30 mL/min.

Dosing of metformin is750–1000 mg BiD p.o. Maximum metformin dosing is 2.55 g/day.

3.2.7 Other Options

Other ongoing trials in order to decrease postburn hyperglycemia include the use of glucagon-like peptide (GLP)-1 and PPAR-γ agonists (e.g., pioglitazone, thioglitazones) or the combination of various anti-diabetic drugs. PPAR-γ agonists, such as fenofibrate, have been shown to improve insulin sensitivity in patients with diabetes. Cree and colleagues found in a recent double-blind, prospective, placebo-controlled randomized trial that fenofibrate treatment significantly decreased plasma glucose significantly decreased plasma glucose concentrations by improving insulin sensitivity and mitochondrial glucose oxidation [53]. Fenofibrate also led to significantly increased tyrosine phosphorylation of the insulin receptor (IR) and IRS-1 in muscle tissue after hyperinsulinemic-euglycemic clamp when compared to placebo-treated patients, indicating improved insulin receptor signaling [53].

GLP-1 has been shown to decrease glucose in severely burned patients, but it was also shown that GLP-1 may not be sufficient to decrease glucose by itself and insulin needs to be given as an adjunct.

4 Summary and Conclusion

The profound metabolic alterations post-burn associated with persistent changes in glucose and lipid metabolism and impaired insulin sensitivity significantly contribute to adverse outcome of this patient population. Even though advances in therapy strategies in order to attenuate the hypermetabolic response to burn have significantly improved the clinical outcome of these patients over the past years, therapeutic approaches to overcome this persistent hypermetabolism and associated hyperglycemia have remained challenging. Early excision and closure of the burn wound has been probably the single greatest advancement in the treating patients with severe thermal injuries during the last 20 years, leading to substantially reduced resting energy requirements and subsequent improvement of mortality rates in this particular patient population. At present, beta-adrenergic blockade with propranolol represents probably the most efficacious anti-catabolic therapy in the treatment of burns. Other pharmacological strategies that have been successfully utilized in order to attenuate the hypermetabolic response to burn injury include growth hormone, insulin-like growth factor, and oxandrolone. Maintaining blood glucose at levels below 130 mg/dL using intensive insulin therapy has been shown to reduce mortality and morbidity in critically ill patients, however, associated hypoglycemic events have led to the investigation of alternative strategies, including the use of metformin and the PPAR-γ agonist fenofibrate. Nevertheless, further studies are warranted to determine ideal glucose ranges and the safety and the appropriate use of the above-mentioned drugs in critically ill patients.

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Considerations for Pain Management in the Burn-Injured Patient

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1 Introduction

Pain has been defined as a "mutually recognizable somatic experience that reflects a person's apprehension of threat to their bodily or existential integrity." [1]. Under normal circumstances, pain helps the body to respond to a source of danger or tissue damage and facilitates protection for tissue repair. Acute pain arises from a range of noxious stimuli, including physical (heat, cold, electrical), mechanical, and chemical [2].

Burn pain has been investigated meticulously in the clinical and research field as the model to understand the intricate pathophysiology processes of pain. Burn pain combines features of nociceptive, neuropathic, and inflammatory mechanism together with peripheral and central components [2, 3].

The management of postburn pain is exceedingly complex, for once it depends on the patient factors such as physical, biological, and social status, but also the burn characteristics and mechanisms of injury. Furthermore, burn pain varies in the same individual throughout the different phases of recovery. Table 1 describes the effects of burns physiology on pain management.

Burn pain can be separated into four components—background pain, procedural pain, breakthrough pain, and neuropathic pain [4]—each of them requiring specific interventions.

Untreated or inadequately treated pain can lead to anxiety, fear, depression, and posttraumatic stress disorder. It can cause peripheral and central sensitization [5], resulting in chronic pain [6]. Lastly, pain can also impair the healing process due to multiple factors, including metabolic, humoral, endocrine, and immunological derangements.

Management of burn pain requires a multimodal management strategy. Despite the current "opioid crisis" and concerns about opioid tolerance, opioid-induced hyperalgesia, opioid abuse, misuse and diversion, intravenous opioids are the cornerstone of burn pain management [7, 8].This chapter will evaluate the pharmacological approach to burn pain. Non-pharmacological interventions, although important, are beyond the scope of this review.

2 Pain Pathways

After stimulation of local nociceptors, the impulse travels via Ad and C fibers to the dorsal horn of the spinal cord. Peripheral sensory nerves and descending influences from cortical areas can modulate the magnitude of the pain impulse. Pain is a conscious experience, an interpretation of the nociceptive input influenced by memories, emotional, pathological,

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Table 1 Effects of burns physiology on pain management

Physiologic state	Effect	Implications
Burn shock (0–48 h)	Plasma protein loss through burned skin Dilution of plasma proteins by resuscitation fluids decreased concentration of albumin Cardiac output decreases Increase pulmonary vascular resistance [39]	Increase in volume of distribution of medications. Elimination of some drugs by the kidney and liver is decreased [42]
Hypermetabolic state with increase blood flow to liver and kidney Generalized edema	Increase clearance and biotransformation of medications Decrease in albumin (binds acid and neutral drugs) Increase in alpha-1-acid glycoprotein (binds cationic drugs)	Increased analgesic clearance and pain [42] Doses and intervals are affected (usually increased doses and shorter intervals) Unpredictable absorption of IM medications Succinylcholine is contraindicated
Cytokine-mediated inflammatory response	Cascade of irritants that sensitize and stimulate pain fibers [3]	Wounds may become primarily hyperalgesic to mechanical or thermal stimuli

genetic, and cognitive factors. Resultant pain is therefore not always related linearly to the nociceptive drive or input, neither is it solely for vital protective functions [9].

Pain is a highly subjective experience affected not only by the burn wound itself but also by context, cognition, pharmacologic, mood, and other predisposing factors [10].

Figure 1 shows a representation of the substances involved in the transmission of noxious stimuli and the possible targets for pharmacological interventions [11].

3 Components of Burn Pain

Burn pain has four distinct components—background, procedural, breakthrough, and neuropathic pain. When pain persists for more than 6 months, it becomes chronic pain. Pharmacological and non-pharmacological interventions should be individualized to target each pain pattern [12].

Table 2 describes the most common pharmacologic interventions, intial doses, side effects, and target pain pattern.

3.1 Background Pain

It is a constant pain that is present while the patient is at rest. Background pain is the result of either direct injury or inflammation of the skin, subcutaneous tissue, muscle, or visceral tissue. This type of pain is typical of low to moderate intensity and long duration. It is best treated with mild-to-moderately potent analgesics administered so that plasma drug concentrations remain relatively constant throughout the day. Pain management strategies typically include regular acetaminophen, regular NSAIDs where appropriate, and the use of long-acting opioids.

3.2 Procedural Pain

In contrast to background pain, procedural pain reaches quite intense levels for a brief period; therefore, analgesic regimens for procedural pain are best comprised of combinations of short-acting opioids, benzodiazepines, magnesium and lidocaine infusions, and subanesthetic doses of ketamine.

Among the short-acting opioids, sufentanil poses particular characteristics that make it the first choice. For once, its potency, solubility, and high affinity for mu receptors. This later characteristic is very important in the context of downregulation of mu and kappa receptors.

Procedural pain is generated by a myriad of interventions such as wound debridement, burn excision, donor skin harvesting, grafting, placement of central lines, dressing changes, and rehabilitation efforts.

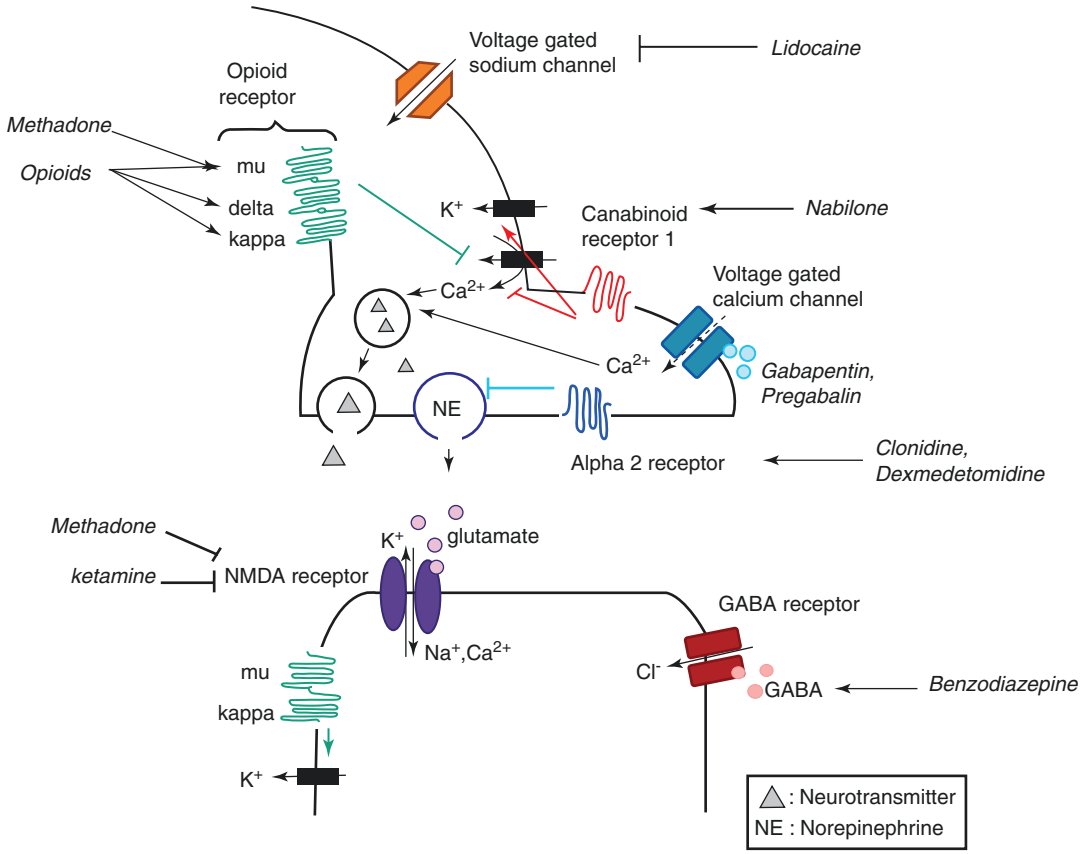

Fig. 1 Pain pathways. *GABA* γ-aminobutyric acid, *NMDA* N-methyl-D-aspartate. Reproduced with permission from Retrouvey H, Shahrokhi S. Pain and the Thermally Injured Patient—A Review of Current Therapies. *Journal of Burn Care & Research*. 2015;36(2):315–323

3.3 Breakthrough Pain

Breakthrough pain describes unexpected spikes of pain that occur when background analgesic effects are exceeded, either at rest, during procedures, or with stress [10]. It can be a result of inadequate doses of analgesics for background pain, or to changing mechanisms of pain over time [13].

3.4 Neuropathic Pain

Neuropathic pain is caused by the direct injury or inflammation to neural tissue or vasum-nevorums in the peripheral and central nervous system. As neurons regenerate, abnormal excitability at or near the site of nerve injury can occur. It often persists after burn wounds have healed. It may be experienced as numbness and tingling in the burned areas, which may progress to painful paresthesias [14].

Since limited options are available for the management of neuropathic pain, gabapentinoids, and laser therapy should be considered as potential treatment options [15].

4 Pain Management

4.1 Pharmacological

4.1.1 Opioids

Opioids mimic the effects of endogenous opioid peptides by interacting with the mu, delta, and kappa receptors. Each opioid has a different

Table 2 Pharmacological options for treatment of burn pain

Medication	Receptor/Mechanism	Dose	Effect	Side Effects	Component of pain target
Opioids	mu, delta, and kappa opioid receptors		Analgesia	Nausea, vomiting, constipation, gastric dysmotility, dependence, and tolerance. Opioid-induced hyperalgesia	Background Procedural Breakthrough
Morphine		IV PCA 1–2 mg Q 5–10 min			
Hydromorphone		PO: 2–4 mg Q2h IV PCA 0.1–0.4 mg Q5–10 min			
Fentanyl		IV PCA 20–50 mcg Q5–10 min			
Sufentanil		IV PCA 2–6 mcg Q5–10 min			
Methadone [17]	Mu opioid (agonist) *NMDA* (antagonist)	15 mg PO OD	Inhibits opioid tolerance and reduces central sensitization	Long half-life (8–59 h)	Background
Oxycodone		10–20 mg POQID			
Codeine		60 mg PO QID			
NSAIDs	Inhibition Cyclo-oxygenase (COX-1 and COX-2).		Antipyretic, anti-inflammatory, and analgesic effects	GI bleeding, decreased platelet activity, and AKI	Background Breakthrough
Acetaminophen	Inhibition of central prostaglandin synthesis	1 g PO QID	Decreases opioid consumption Synergistic effects with opioids		Background Breakthrough

Antidepressants [15]	Interference with serotonin uptake, interaction with alpha-receptors, opioidergic effect, blockade of NMDA receptor, sodium and calcium channel. Inhibition of histaminic, cholinergic, muscarinic, and nicotinic receptors			Anticholinergic effects (tachycardia, dry mouth, urinary retention), sedation	
Amitriptyline		10–50 mg PO QHS			Neuropatic
Duloxetine	SNRIs	30–120 mg PO OD			Neuropatic
Dexmedetomidine [24]	α-2 agonist (2A subtype)	0.2–0.7 mcg/kg/h	Minimal to no risk of respiratory depression	Bradycardia and hypotension	Procedural
Clonidine [22]	α-2 agonist	0.1 mg PO BID		Bradycardia and hypotension	Procedural
Lidocaine [34]	Voltage-gated sodium channels	1 mg/kg/H	Inhibiting nerve conduction in afferent nerves that signal pain	Seizures, arrhythmias, bradycardia	Procedural Background
Cannabinoids	CB1 (responsible for most side effects) CB2 (responsible for non-psychotropic effects)		Anti-inflammatory and anti-hyperalgesia	Dependence, tolerance, headache, dizziness, anxiety, memory impairment, speech impediment, and sedation	Neuropathic
Nabilone [30]	CB 1 agonist	0.5–1 mg PO BID			
Gabapentinoids [25]	α2δ-1 subunit of voltage-gated calcium channels (dorsal horn and dorsal root ganglia)		Inhibits the sensitization of the central nervous system by reducing neurotransmitter release Reduce postburn pruritus	Dizziness, somnolence, dry mouth, and edema	Neuropathic
Pregabalin		25–200 mg PO TID			
Gabapentin		100–1200 mg PO TID			
Benzodiazepines	GABA receptor		No analgesic properties	Sedation, respiratory depression, addiction, and tolerance	Procedural Background
Lorazepam		1–2 mg PO			

(continued)

Table 2 (continued)

Medication	Receptor/Mechanism	Dose	Effect	Side Effects	Component of pain target
Midazolam		1–3 mg IV			
Ketamine [20]	NMDA (antagonist)	IV: 0.1–0.3 mg/kg/h PO 30–90 mg QID	Blocks pain transmission by inhibiting central sensitization Reduce primary and secondary hyperalgesia [21] Increases thermal injury-induced mechanical pain thresholds	Nausea, vomiting, hallucinations, mood alteration, bizarre dreams, emergence delirium Sympathetic activation causes tachycardia, hypertension, and salivation	Background Procedural Breakthrough
Nitrous Oxide [41]	Promotes the release of endogenous opioids that activate GABA Supraspinal GABA inhibition Spinal GABA activation	50–65% N_2O		Nausea, vomiting, hypoxia, vit B12 deficiency	Procedural
Magnesium		20–50 mcg/kg/h (max 2 g/h/max 24 h)			Neuropathic

AKI acute kidney injury, *GABA* γ-aminobutyric acid, *GI* gastrointestinal, *NMDA N*-methyl-D-aspartate receptor antagonist, *CB* Cannabinoid, *PCA* Patient-controlled analgesia, *SNRIs* Serotonin and norepinephrine receptor inhibitors, *OD* once a day, *QHS* once at night, *BID* twice a day, *TID* three times a day, *QID* four times a day, *PO* oral

effect on these subtypes of receptors, but mostly activate the mu receptor. The wide spectrum of opioids available for clinical use provides dosing flexibility (i.e., variable routes of administration, variable duration of action, variable potency) [13, 16].

For hospitalized burn patients, opioids are the cornerstone of pharmacologic pain control, in part because they are potent, inexpensive, widely available, and familiar to the majority of health care providers [12].

Side effects of opioids are significant and include respiratory depression, constipation, sedation, pruritus, sleep cycle interference, nausea, hallucinations, and vomiting. Additionally, opioids have been associated with dependence, tolerance, and hyperalgesia.

The opioid agonist-antagonist drugs (e.g., nalbuphine, butorphanol) produce analgesia (agonist property) with lesser side effects (antagonist properties), but also exhibit ceiling effects, limiting its use to mild burn pain.

Opioids are not effective at treating neuropathic burn pain.

Range doses for the most commonly used opioids are detailed in Table 2. Suggested starting doses are:

- Morphine: PCA 1 mg lockout 10 min.
- Hydromorphone: PCA 0.1 mg lockout 10 min. PO 2 mg Q2H.
- Fentanyl: PCA 25 mcg lockout 10 min.
- Sufentanil: PCA 2 mcg lockout 10 min.
- Oxycodone: 20 mg PO Q6H.
- Codeine: 60 mg PO Q6H.

Methadone

Methadone is a mu opioid receptor agonist with a weak NMDA receptor antagonist. Methadone is a moderate analgesic that has been used as an alternative analgesic in opioid-tolerant patients and to treat opioid dependence [17].

- The suggested starting dose is 15 mg PO once a day.

4.1.2 Adjuvants

NSAIDs

NSAIDs cause analgesia and anti-inflammatory effects by inhibition of prostaglandin synthesis by the cyclo-oxygenase (COX-1 and COX-2) [18].

NSAIDs are mild analgesics that exhibit a ceiling effect in their dose–response relationship. They are useful as adjuncts to opioids treating minor burns, usually in the outpatient setting. NSAIDs had shown to decrease central hyperalgesia, have a synergistic effect, and are opioid-sparing.

The widespread inhibition of cyclo-oxygenase is responsible for many of the adverse effects of these NSAIDs. Bleeding risk, gastrointestinal complications, and renal toxicity are the most feared side effects; making these agents generally unsuitable for the treatment of the typical, severe burn pain [10].

The suggested starting dose is:

- Celecoxib: 200 mg PO loading dose, followed by 100 mg PO Q12H (maximum 4 days).
- Ketorolac: 15 mg IV loading dose, followed by 7.5 mg IV Q6H (maximum 4 days).

Acetaminophen

Acetaminophen is an antipyretic and an analgesic with both central and peripheral pain modulation activity. The mechanism of action of acetaminophen is unknown, but it may involve the inhibition of central prostaglandin synthesis and the activation of descending serotonergic pathways [19].

Acetaminophen is usually administered as an adjunct to opioids for major burns as it has a synergistic effect.

- The suggested starting dose is 1 g PO Q6H.

Ketamine

Ketamine is an NMDA (N-methyl- d-aspartate) receptor antagonist used as a dissociative anes-

thetic and adjunct pain medication [20]. Ketamine acts on the thalamic function and the limbic system as a potent noncompetitive NMDA receptor antagonist and inhibits central pathways associated with central and peripheral pain sensitization [21].

Ketamine has many potential advantages for the induction and maintenance of anesthesia in burn patients such as hemodynamic stability, preserving airway patency as well as hypoxic and hypercapnic responses, and decreasing airway resistance.

The suggested starting dose is:

- Intravenous infusion: 0.1 mg/kg/H. Preferred route.
- Oral: 30 mg Q6H. Low bioavailability.

Alfa Antagonist

Clonidine

Clonidine is an α-2 agonist used for its sedative, anxiolytic, and analgesic properties. It is useful as an adjunct as it enhances opioid analgesia, decreases opioid requirement, and prolongs local anesthetic action [22]. It can also be administered in the management of alcohol, opiate, and nicotine withdrawal.

- The suggested starting dose is 0.1 g PO Q12H.

Dexmedetomidine

Dexmedetomidine has specificity to the 2A subtype of the alpha-2 receptor, causing it to be a more effective sedative and analgesic than clonidine.

Dexmedetomidine has been used to provide sedation–analgesia for burned patients and to decrease opioid requirements [23]. Titration of dexmedetomidine may also allow weaning of benzodiazepine as patients get close to extubation. Dexmedetomidine has been shown to result in less delirium than benzodiazepines in several critical care studies [24]. However, it can cause hypotension at higher doses in the presence of hypovolemia, therefore, should not be given to hemodynamically unstable patients.

- The suggested starting intravenous infusion is 0.2 mcg/kg/h.

Gabapentinoids

Gabapentin

Gabapentin is a structural analog of GABA. Its mechanism of action is not fully defined, but it involves inhibition of the release of excitatory neurotransmitters and increases the release of inhibitory neurotransmitter GABA by binding to the alpha-2-delta-1 subunit of the voltage-gated calcium channel [25].

Gabapentin has been used to manage chronic neuropathic burn pain because it inhibits the central sensitization of pain and also relives postburn pruritus.

- The suggested starting dose is 100 mg PO Q8H.

Pregabalin

Like Gabapentin, Pregabalin binds to the alpha-2-delta-1 subunit of the presynaptic voltage-gated calcium channel in the dorsal horn of the spinal cord, with subsequent reduced release of the excitatory neurotransmitter glutamate. It has both analgesic and anxiolytic properties [4, 25].

- The suggested starting dose is 50–100 mg PO Q12H.

Cannabinoids

The *Cannabis sativa* plant contains over 100 bioactive lipid compounds, known as cannabinoids, which produce analgesia in animal models of acute and chronic pain. However, due to abuse potential and numerous additional side effects, such as dependence, tolerance, hypomotility, deficits in executive function, and memory consolidation, the use of cannabis for medicinal purposes has been restricted until recent times [26].

There are two types of cannabinoid (CB) receptors. The CB1 receptor which is found both in the periphery and central nervous system (CNS), and CB2 receptor which is typically expressed predominantly by cells of the immune system, including glial cells of the CNS [27].

The undesirable effects of cannabinoids are caused by the global activation of CNS CB1 receptors. Current research has focused on presumed site-specific modulation of endogenous ligand activity or effects at the non-psychotropic CB2 receptor.

Cannabinoids have been studied in the management of chronic and neuropathic pain in the nonburn population [15, 28].

Currently, the synthetic cannabinoids agents dronabinol [29] (synthetic delta-9-tetrahydrocannabinol), tetrahydrocannabinol, and cannabidiol (CBD) sprays are not FDA-approved for analgesia but are available in the United States.

Nabilone (Cesamet)

Nabilone is a synthetic CB1 and CB2 agonist. The mechanism of pain modulation by nabilone is complex and involves the peripheral afferent nerves, the dorsal root ganglia, and spinal dorsal horn as well as specific brain areas [30]. Nabilone is effective at decreasing pain and anxiety as well as improving sleep.

- The suggested starting dose is 0.5 mg PO Q12H.

Nitrous Oxide

Nitrous oxide is an inhalant anesthetic that has modest analgesic properties when delivered at subanesthetic doses [31]. Inhaled nitrous oxide and oxygen mixtures can be a very useful form of analgesia for short procedures, such as dressing changes as it has a rapid onset (within seconds) and short duration of action. Although it is generally well-tolerated, nitrous oxide can cause nausea and vomiting, precluding its use in some patients. Repeated or prolonged administration of nitrous oxide can interfere with vitamin B12 metabolism, causing serious hematological and neurological adverse effects and necessitating monitoring and vitamin B12 supplementation as required.

- The suggested starting dose is mixures of 50% N_2O.

Benzodiazepines

Benzodiazepines act by amplifying GABA in the central nervous system, and by reducing catecholamines in the peripheral nervous system.

Although not considered analgesic, benzodiazepines can be effective in alleviating pain symptoms in combination with other analgesics, most likely due to their sedative and anxiolytic effects. Benzodiazepines, with a short-to-moderate duration of action, such as midazolam and lorazepam, are preferred to longer-acting drugs [32].

Benzodiazepines administered along with ketamine can reduce dysphoria. When administered as an adjunct to opioids, benzodiazepines have been shown to decrease both background pain and pain in those patients with high levels of procedural pain [12].

The suggested starting dose is:

- Lorazepam: 1 mg PO.
- Midazolam: 1 mg IV.

Lidocaine

Lidocaine acts on the voltage-gated sodium channels by blocking the inflow of sodium, causing inhibition in the propagation of the action potentials in neurons [33].

Lidocaine can be used as a local, topical, or systemic anesthetic. However, topical use has been associated with toxicity due to rapid systemic absorption. The efficacy of Lidocaine as an intravenous infusion for the treatment of central and peripheral sensitization as well as neuropathic pain is still being investigated [34].

- The suggested starting intravenous infusion is 1 mg/kg/h.

Antidepressants

Posttraumatic stress disorder and depression has been reported to occur in up to 30% of patients with severe burn injury, often developing in the setting of inadequate treatment of anxiety and pain [35].

Tricyclic antidepressants and serotonin-norepinephrine reuptake inhibitors, appear to enhance opiate-induced analgesia, especially in

patients with neuropathic pain. In addition, antidepressants can help to manage the depression, anxiety, and insomnia that frequently accompany severe burn injury [15].

Due to the potential risk of toxicity, it is essential to monitor the patient for signs of serotoninergic syndrome and cardiac arrhythmias.

The suggested starting dose is:

- Amitriptyline: 20 mg PO at night.
- Duloxetine: 30 mg PO once a day.

Magnesium

Magnesium is a weak non-selective NMDA receptor antagonist that is involved in neuromodulation of central and peripheral excitability and sensitization. Also, it enhances and promotes mu receptor upregulation, which is very useful in opioid tolerance and opioid induce hyperalgesic states.

- The suggested starting intravenous infusion is 20 mcg/kg/h. Maximum 2 g/h for a maximum of 24 h.

4.2 Regional Anesthesia

- Regional anesthesia has an important role in the intraoperative management of burn patients because it provides anesthesia in the operating room, can offer postoperative pain control, and facilitates rehabilitation. Regional anesthesia should be considered both for burn wound pain and donor site pain [10].
- There are several forms of regional anesthesia, starting from simple techniques such as tumescent local anesthesia injected into a donor site before harvesting [36], subcutaneous catheter infusions [37], or more complex techniques such as peripheral nerve, or central neuraxial blocks [38].
- Central neuraxial techniques (spinal, epidural) have been used with good effect. There are no reports suggesting that epidural abscesses are more common in burn patients, but studies have suggested that intravascular catheters are more likely to become infected if placed in or near burned tissue [39].
- The lateral femoral cutaneous nerve block is an excellent target for blocks because it is exclusively a sensory nerve and innervates the lateral thigh, which is frequently chosen for split-thickness skin grafts. A fascia iliaca block can also be performed if there is a need to cover the anterior and medial thigh [37, 38, 40].

4.3 Non-pharmacological

Factors such as depression or anxiety strongly affect the perception of pain in burn patients. Although pharmacological agents targeted to control pain are important, non- pharmacological therapies are essential adjuncts for optimal pain control [15].

It is beyond the scope of this chapter to review the indication and evidence of non-pharmacological interventions. Table 3 lists the most common non-pharmacological interventions.

5 Summary

- The management of burn pain is exceedingly complex as it is affected by patient factors, burn characteristics, and mechanisms of injury.
- Burn pain will vary in the same individual throughout the different phases of recovery.

Table 3 Non-pharmacological interventions

Acupuncture
Aromatherapy
Biofeedback
Cognitive-behavioral therapy
Cooling
Extracorporeal shock wave therapy
Hypnosis
Interactive gaming console
Massage
Mindfulness
Music
Laser therapy
Noncontact low-frequency ultrasound
Transcranial direct current stimulation
Transcutaneous electrical nerve stimulation
Virtual reality/augmented reality
Whole-body vibration

Therefore, analgesic regimens should be continuously evaluated and adjusted accordingly.
- An adequate pain control has severe short- and long-term consequences in the patient journey to recovery.
- Despite the side effects and potential for dependence and misuse, opioids are the cornerstone of pharmacologic pain control.
- Management of burn pain requires a multimodal approach strategy, including pharmacological and non-pharmacological modalities.
- Chronic and neuropathic pain are common sequelae in burn patients. Cannabinoids had shown promissing results in recent studies, but further investigation is required.

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Nursing Care of the Burn Patient

Judy Knighton

1 Introduction

The repertoire of skills needed to provide optimal nursing care to the burn-injured patient includes comprehensive clinical assessment and monitoring, pain management, wound care and psychosocial support. This chapter is focused on providing the nurse with evidence-based information to guide the provision of such care.

2 Knowledge Base

2.1 General Definition and Description

2.1.1 Incidence

- Annually, an estimated 486,000 people in the USA [1], 55,000 in Canada [2], and nearly 11 million people around the world [3] seek care for burn injuries.
- Approximately 40,000 require hospitalisation, greater than half of whom (25,000) receive care in specialised burn units or centres [1].
- Survival rate, for hospitalised patients, is around 96%.
- The majority of patients, who die from their injuries (approximately 180,000), are from low- and middle-income countries [3].
- Children less than 5 years of age and adults over the age of 64 form the largest group of fatalities [4–6].
- In North America and Europe, 70% of burn survivors are male and 30% female [7].

2.1.2 Classification

Burn complexity can range from a relatively minor, uncomplicated injury to a life-threatening, multisystem trauma. The American Burn Association (ABA) has a useful classification system that rates burn injury magnitude from minor to moderate, uncomplicated to major (Table 1).

3 Aetiology and Risk Factors

The causes of burn injuries are numerous and found in both the home, leisure and workplace settings (Table 2).

3.1 Pathophysiology

3.1.1 Severity Factors

There are five factors that need to be considered when determining the severity of a burn injury (Box 1):

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Table 1 American Burn Association adult burn classification

Classification	Assessment criteria
Minor burn injury	<15% TBSA burn in adults <40 years age
	<10% TBSA burn in adults >40 years age
	<2% TBSA full-thickness burn without risk of functional or aesthetic impairment or disability
Moderate uncomplicated burn injury	15–25% TBSA burn in adults <40 years age
	10–20% TBSA burn in adults >40 years age
	<10% TBSA full-thickness burn without functional or aesthetic risk to burns involving the face, eyes, ears, hands, feet or perineum
Major burn injury	>25% TBSA burn in adults <40 years age
	>20% TBSA burn in adults >40 years age
	OR > 10% TBSA full-thickness burn (any age)
	OR injuries involving the face, eyes, ears, hands, feet
	OR perineum likely to result in functional or aesthetic disability
	OR high-voltage electrical burn
	OR all burns with inhalation injury or major trauma

Table 2 Causes of burn injuries

Home and leisure	Workplace
Hot water heaters set too high (140 °F or 60 °C)	Electricity:
Overloaded electrical outlets	Power lines
Frayed electrical wiring	Outlet boxes
Carelessness with cigarettes, e-cigarettes, lighters, matches, candles	Chemicals:
Pressure cookers	Acids
Microwaved foods and liquids	Alkalis
Hot grease or cooking liquids	Tar
Open space heaters	Hot steam sources:
Gas fireplace doors	Boilers
Radiators	Pipes
Hot sauna rocks	Industrial cookers
Improper use of flammable liquids:	Hot industrial presses
Starter fluids	Flammable liquids:
Gasoline	Propane
Kerosene	Acetylene
Electrical storms	Natural gas
Overexposure to sun	

Box 1: Burn Severity Factors

1. Extent of body surface area burned
2. Depth of tissue damage
3. Age of person
4. Part of body burned
5. Past medical history

1. *Extent*—Several methods are currently available to accurately calculate the percentage of body surface area involved [8–11]:
   (a) The simplest is the rule of nines (see Chap. 1, Fig. 1 and Chap. 2, Fig. 2). *However, it is only for use with the adult burn population.*
   (b) The Lund and Browder method (see Chap. 1, Fig. 1 and Chap. 2, Fig. 2) is useful for all age groups, but is more complicated to use.
   (c) There is a paediatric version of the Lund and Browder method (see Chap. 2, Fig. 2).
   (d) If the burned areas are scattered, small and irregularly shaped, the area of the open hand (including the palm and extended fingers) can be used. This area of the burned person's hand represents 1% body surface area.
   (e) If 10% or more of the body surface of a child or 15% or more of that of an adult is burned, the injury is considered serious. The person requires hospitalisation and fluid replacement to prevent shock.
2. Depth
   (a) Two factors determine the depth of a burn wound: temperature of the burning agent and duration of exposure time.

Table 3 Classification of burn injury depth

Degree of burn	Cause of injury	Depth of injury	Appearance	Treatment
First degree	Superficial sunburn	Superficial damage to epithelium	Erythematous, blanching on pressure, no blisters	Complete healing within 3–5 days with no scarring
	Brief exposure to hot liquids or heat flash	Tactile and pain sensations intact		
Superficial partial-thickness (second degree)	Brief exposure to flame, flash or hot liquids	Destruction of epidermis, superficial damage to upper layer of dermis, epidermal appendages intact	Moist, weepy, blanching on pressure, blisters, pink or red colour	Complete healing within 14–21 days with no scarring
Deep partial-thickness (deep second degree)	Exposure to flame, scalding liquids or hot tar	Destruction of epidermis, damage to dermis, some epidermal appendages intact	Pale and less moist, no blanching or prolonged, deep pressure sensation intact, pinprick sensation absent	Prolonged healing time usually >21 days with scarring. Skin grafting may be necessary for improved functional and aesthetic outcome
Full-thickness (third degree)	Prolonged contact with flame, steam, scalding liquids, hot objects, chemicals or electrical current	Complete destruction of epidermis, dermis and epidermal appendages; injury through most of the dermis	Dry, leathery, pale, mottled brown or red in colour; visible thrombosed vessels insensitive to pain and pressure	Requires skin grafting
Full-thickness (fourth degree)	Major electrical current, prolonged contact with heat source (i.e. unconscious patient)	Complete destruction of epidermis, dermis and epidermal appendages; injury involving connective tissue, muscle and bone	Dry, black, mottled brown, white or red; no sensation and limited movement of burned limbs or digits	Requires skin grafting and likely amputation

(b) At the present time, visualisation with the naked eye is used to determine burn depth. However, there is ongoing research exploring the use of newer laser technologies to determine burn depth [12].
(c) Previous terminology to describe burn depth was first, second and third degree. In recent years, these terms have been replaced by those more descriptive in nature: superficial partial-thickness, deep partial-thickness and full-thickness (Table 3).
(d) Superficial burns, such as those produced by sunburn, are not taken into consideration when assessing extent and depth.
(e) The skin is divided into three layers, which include the epidermis, dermis and subcutaneous tissue (Fig. 1).

3. Age
   (a) For patients less than 5 years of age and greater than 64, there is a higher incidence of morbidity and mortality.
   (b) Sadly, the infant, toddler and elderly are at increased risk for abuse by burning.
4. Part of the body burned.
   (a) Patients with burns to the face, neck, hands, feet or perineum have greater challenges to overcome and require the specialised care offered by a burn centre.

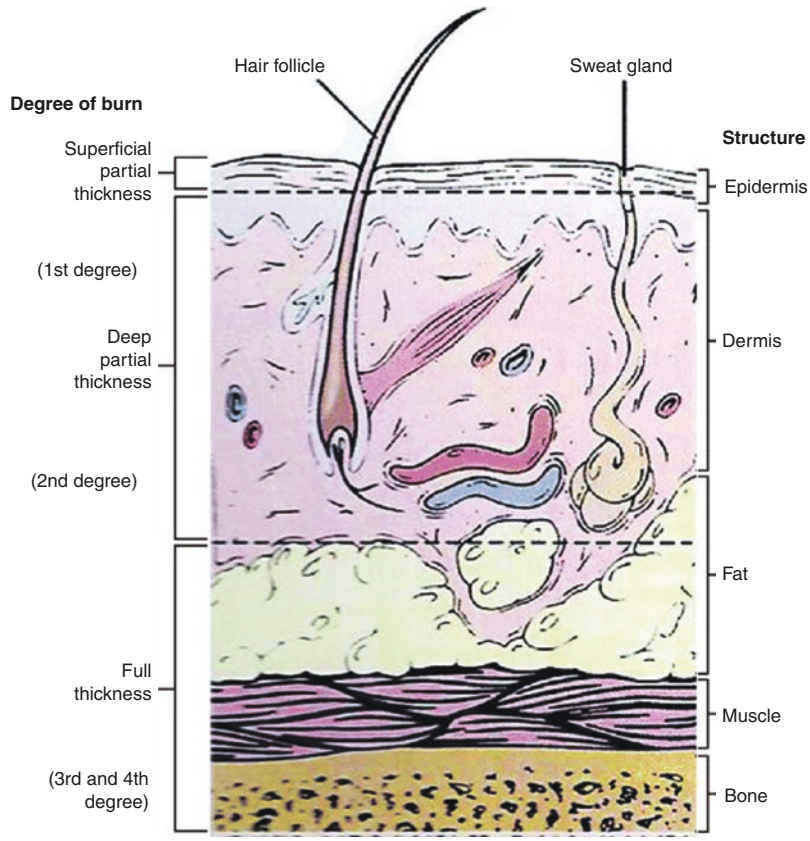

Fig. 1 Anatomy of burn tissue depth

5. Past medical history
   (a) Pre-existing cardiovascular, pulmonary or renal disease will be exacerbated by the burn injury.
   (b) Persons with diabetes or peripheral vascular disease have a more difficult time with wound healing, especially on the legs and feet [13, 14].

3.2 Local Damage

Local damage varies, depending upon:

(a) Temperature of the burning agent.
(b) Duration of contact time.
(c) Type of tissue involved.

Zones of tissue damage:

- Inner zone of *coagulation* (full-thickness injury)—irreversible cell death, skin grafting needed for permanent coverage
- Middle zone of *stasis* (deep, partial-thickness injury)—some skin-reproducing cells present in the dermal appendages with circulation partially intact, healing generally within 14–21 days
- Outer zone of *hyperaemia* (superficial, partial-thickness injury)—minimal cell involvement and spontaneous healing within 7–10 days

3.3 Fluid and Electrolyte Shifts

The immediate post-burn period is marked by dramatic circulation changes, producing what is known as "burn shock" (Fig. 2).

- As the capillary walls begin leaking, water, sodium and plasma proteins (primarily albumin) move into the interstitial spaces in a phenomenon known as "second spacing".
- When the fluid begins to accumulate in areas where there is normally minimal to no fluid,

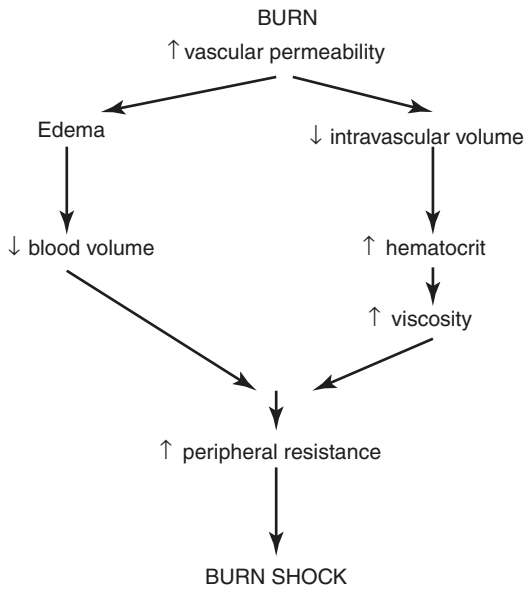

Fig. 2 Burn shock

the term "third spacing" is used. This fluid is found in exudate and blisters.

- There is also insensible fluid loss through evaporation from large, open body surfaces. A non-burned individual loses about 30–50 mL/h. A severely burned patient may lose anywhere from 200 to 400 mL/h.
- Circulation is also impaired in the burn patient due to haemolysis of red blood cells.
- Following successful completion of the fluid resuscitation phase, capillary membrane permeability is restored. Fluids gradually shift back from the interstitial space to the intravascular space, and the patient is no longer grossly oedematous and diuresis is ongoing.

4 Cardiovascular, Gastrointestinal and Renal System Manifestations

During the hypovolemic shock phase, only vital areas of circulation are maintained.

- Cardiac monitoring is essential, particularly if the patient has a pre-burn history of cardiac problems.
- Electrical burn patients, who arrest at the scene or who experience cardiac arrhythmias post-injury, warrant particular vigilance.
- Hypovolemic shock and hypoxemia also produce the initial gastrointestinal complications seen post-burn, such as decreased peristalsis and abdominal paralytic ileus.
- Stress response post-burn releases catecholamines and may produce stress (Curling's) ulcers in burns >50% body surface area.
- Renal complications are predominantly caused by hypovolemia. If perfusion remains poor, high circulating levels of haemoglobin and myoglobin may clog the renal tubules, causing acute tubular necrosis.

4.1 Types of Burn Injuries

- *Thermal* (Table 4)
  - Dry heat, such as flame and flash
  - Moist heat, such as steam and hot liquids
  - Direct contact, such as hot surfaces and objects
  - Major source of morbidity and mortality across all age groups (Figs. 3 and 4)
- *Chemical* (Fig. 5)
  - More than 25,000 chemicals worldwide
  - Divided into two major groups: acids and alkalis
  - Extent and depth injury: directly proportional to the amount, type and strength of

Table 4 Causes of thermal burns

Cause	Examples
Dry heat—flame	Clothing catches on fire Skin exposed to direct flame
Dry heat—flash	Flame burn associated with explosion (combustible fuels)
Moist heat—hot liquids (scalds)	Bath water Beverages—coffee, tea, soup Cooking liquids or grease
Moist heat—steam	Pressure cooker Microwaved food Overheated car radiator
Contact—hot surfaces	Oven burner and door Barbecue grill
Contact—hot objects	Tar Curling iron Cooking pots/pans

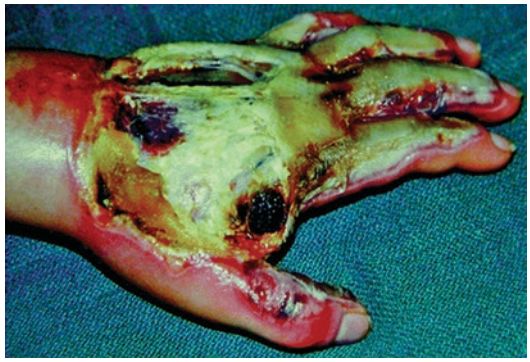

Fig. 3 Third degree/full-thickness flame burn

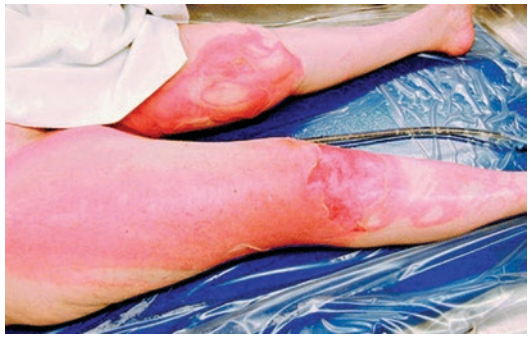

Fig. 4 Scald burn: looks can be deceiving—burn wound progression over several days

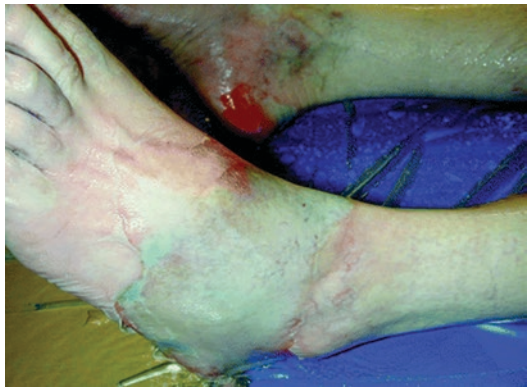

Fig. 5 Chemical burns: looks can be deceiving—copious flushing for up to several hours

the agent, its concentration, degree of penetration, mechanism of action and length of contact time with the skin

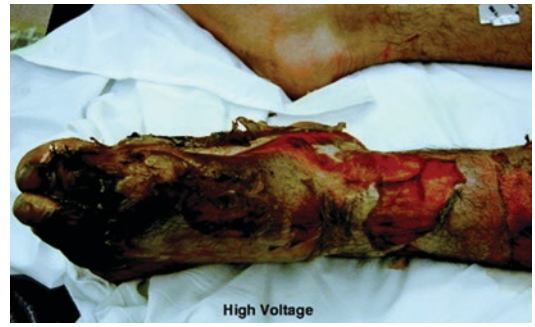

Fig. 6 Electrical burn

- *Electrical* (Fig. 6)
  - Comprise a small portion of the burn population.
  - Outcomes can be devastating due to tissue damage and potential limb loss.
  - Severity of injury difficult to determine as most of the damage may be below skin at level of muscle, fat and bone.
  - Contact points determine probable path of current and potential areas of injury.
  - If the person has fallen post-injury, protect head and cervical spine during transport; need to perform spinal X-rays and neurological assessment.
  - May continue to be at risk for cardiac arrhythmias for 24 h post-burn, so ECG needed on admission and at 24 h post-burn.
  - Infuse Lactated Ringer's solution at a rate that maintains a good urinary output between 75 and 100 mL/h until colour of urine sufficient to suggest adequate dilution of haemoglobin and myoglobin pigments.
  - Administer osmotic diuretic (e.g. mannitol) to establish and maintain acceptable urinary output.
- *Smoke and Inhalation Injury* (Fig. 7).
  - Exposure to smoke and inhalation of hot air, steam or noxious products of combustion.
  - Presence of inhalation injury, with a large burn, can increase a person's mortality rate.

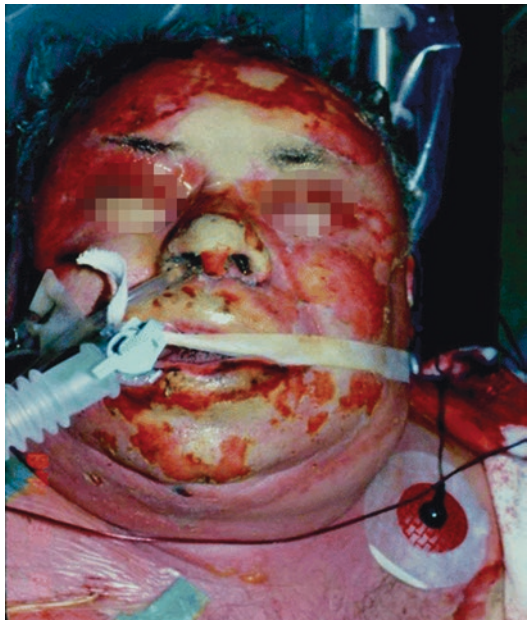

Fig. 7 Inhalation injury

Table 5 Signs and symptoms of carbon monoxide poisoning

Carboxyhaemoglobin saturation (%)	Signs and symptoms
5–10	Visual acuity impairment
11–20	Flushing, headache
21–30	Nausea, impaired dexterity
31–40	Vomiting, dizziness, syncope
41–50	Tachypnoea, tachycardia
>50	Coma, death

  - Signs and symptoms: burns to head and neck, singed nasal hairs, darkened oral and nasal membranes, carbonaceous sputum, stridor, hoarseness, difficulty swallowing, history of being burned in an enclosed space, exposure to flame, including clothing catching fire near the face, indoors and outdoors.
  - Critical period is 24–48 h post-burn.
  - Most fatalities at fire scene caused by carbon monoxide poisoning or asphyxiation (Table 5).
  - Treatment consists of aggressive fluid resuscitation and administration of 100% humidified oxygen until carboxyhaemoglobin falls to acceptable levels.
- *Radiation*
  - Overexposure to sun or radiant heat sources, such as tanning lamps or tanning beds.
  - Nuclear radiation burns require government intervention and specialised treatment.

4.1.1 Clinical Manifestations

Care Priorities During the Emergent, Acute and Rehabilitative Periods

Recovery from a burn injury involves successful passage through three phases of care: emergent, acute and rehabilitative. Recently, recommendations for care have been published to address the educational needs of both non-burn and burn specialists around the world [15]. A number of e-learning applications have made the sharing of evidence-based burn care readily available to health care practitioners, working in a variety of settings around the world [16–19]

1. Principles of care for the *emergent* period: resolution of the immediate problems resulting from the burn injury. The time required for this to occur is usually 1–2 days. The emergent phase ends with the onset of spontaneous diuresis.
2. Principles of care for the *acute* period: avoidance, detection and treatment of complications and wound care. This second phase of care ends when the majority of burn wounds have healed.
3. Principles of care for the *rehabilitative* period: eventual return of the burn survivor to an acceptable place in society and completion of functional and cosmetic reconstruction. This phase ends when there is resolution of any outstanding clinical problems resulting from the burn injury.
   (a) Initial assessment of the burn patient is like that of any trauma patient and can best be remembered by the simple acro-

nym "ABCDEF" (Box 2). During the *emergent period*, burn patients exhibit signs and symptoms of hypovolemic shock (Box 3). Lack of circulating fluid volumes will also result in minimal urinary output and absence of bowel sounds. The patient may also be shivering due to heat loss, pain and anxiety. With inhalation injury, the airway should be examined visually and then with a laryngoscope/bronchoscope (Box 4). The patient may also experience pain, as exhibited by facial grimacing, withdrawing and moaning when touched, particularly if the injuries are partial-thickness in nature. Some areas of full-thickness burn may be anaesthetic to pain and touch if the nerve endings have been destroyed. It is important to examine areas of circumferential full-thickness burn for signs and symptoms of vascular compromise, particularly the extremities (Box 5). Areas of partial-thickness burn appear reddened, blistered and oedematous. Full-thickness burns may be dark red, brown, charred black or white in colour. The texture is tough and leathery, and no blisters are present. If the patient is confused, care providers must determine if it is the result of hypovolemic shock, inhalation injury, substance abuse, pre-existing history or, more rarely, head injury sustained at the time of the trauma. It is essential to immobilise the c-spines until a full assessment can be performed and the c-spines cleared. At this time, a secondary survey assessment is performed (Box 6).

(b) In the *acute phase*, the focus is on *wound care* and *prevention/management of complications*. At this point, the burn wounds should have declared themselves as being partial-thickness or full-thickness in nature. Eschar on partial-thickness wounds is thinner, and, with dressing changes, it should be possible to see evidence of eschar separating from the viable wound bed. Healthy, granulation tissue is apparent on the clean wound bed, and re-epithelialising cells are seen to migrate from the wound edges and the dermal bed to slowly close the wound within 10–14 days. Full-thickness wounds have a thicker, more leathery eschar, which does not separate easily from the viable wound bed. These wounds require surgical excision and grafting. Ongoing assessment of the patient's systemic response to the burn injury continues to be an essential part of an individualised plan of care. Subtle changes quickly identified by the burn team can prevent complications from occurring or worsening over time.

(c) During the final, *rehabilitative phase*, attention turns to *scar maturation, contracture development and functional independence issues*. The areas of burn, which heal either by primary intention or skin grafting, initially appear red or pink and are flat. Layers of re-epithelialising cells continue to form, and collagen fibres in the lower scar tissue add strength to a fragile wound. Over the next month, the scars may become more red from increased blood supply and more raised from disorganised whorls of collagen and fibroblasts/myofibroblasts. The scars are referred to as hypertrophic in nature. If oppositional forces are not applied through splinting devices, exercises or stretching routines, this new tissue **c**ontinues to heal by shortening and forming contractures. A certain amount of contracture development is unavoidable, but the impact can be lessened through prompt and aggressive interventions.

Box 2: Primary Survey Assessment

A	➔	**A**irway
B	➔	**B**reathing
C	➔	**C**irculation
		C-spine immobilisation
		Cardiac status
D	➔	**D**isability
		Neurological **D**eficit
E	➔	**E**xpose and **e**valuate
F	➔	**F**luid resuscitation

Box 3: Signs and Symptoms of Hypovolemic Shock

- Restlessness, anxiety
- Skin—pale, cold, clammy
- Temperature below 37 °C
- Pulse is weak, rapid, ↓ systolic BP
- Urinary output <20 mL/h
- Urine-specific gravity >1.025
- Thirst
- Haematocrit <35; BUN ↑

Box 4: Physical Findings of Inhalation Injury

- Carbonaceous sputum
- Facial burns, singed nasal hairs
- Agitation, tachypnoea, general signs of hypoxemia
- Signs of respiratory difficulty
- Hoarseness, brassy cough
- Rales, ronchi
- Erythema of oropharynx or nasopharynx

Box 5: Signs and Symptoms of Vascular Compromise

- Cyanosis
- Deep tissue pain
- Progressive paraesthesias
- Diminished or absent pulses
- Sensation of cold extremities

Box 6: Secondary Survey Assessment

- Head-to-toe examination
- Rule out associated injuries
- Pertinent history
  - Circumstances of injury
  - Medical history

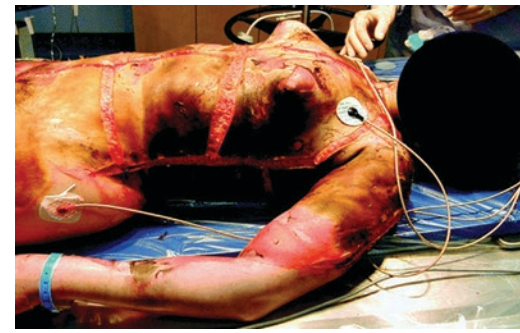

Fig. 8 Full-thickness flame burn with releasing escharotomies

5 Clinical Management

5.1 Nonsurgical Care

Emergent Phase Priorities: airway management, fluid therapy, initial wound care

Emergent Phase Goals of Care: initial assessment, management and stabilisation of the patient during the first 48 h post-burn

Emergent Phase Assessment

- During the rapid, **primary survey**, airway and breathing assume top priority. A compromised airway requires prompt attention and breath sounds verified in each lung field.
- If circumferential, full-thickness burns are present on the upper trunk and back, ventilation must be closely monitored as breathing might be impaired and releasing escharotomies necessary (Fig. 8).
- Spine must be stabilised until c-spines are cleared.
- Circulation is assessed by examining skin colour, sensation, peripheral pulses and capillary filling. Circumferential, full-thickness

burns to the arms or legs must be assessed via palpation or Doppler for evidence of adequate circulation. Escharotomies might be required.
- Typically, burn patients are alert and oriented the first few hours post-burn. If that is not the case, consideration must be given to associated head injury (including a complete neurological assessment), substance abuse, hypoxia or pre-existing medical conditions.
- All clothing and jewellery need to be removed in order to visualise the entire body and avoid the "tourniquet-like" effect of constricting items left in place as oedema increases.
- Adherent clothing needs to be gently soaked off with tepid water or normal saline to avoid further trauma and unnecessary pain.
- Prompt fluid resuscitation must be initiated to address hypovolemic shock.
- The head-to-toe **secondary survey** rules out any associated injuries. Medical problems are identified and managed in a timely fashion.
- Circumstances of the injury must be explored to understand the mechanism, duration and severity of the injury.
- Patient's pertinent medical history includes identification of pre-existing disease or associated illness (cardiac or renal disease, diabetes, hypertension), medication/alcohol/drug history, allergies and tetanus immunisation status. A handy mnemonic can be used to remember this information (Box 7).

Box 7: Secondary Survey Highlights

A	*A*llergies
M	*M*edications
P	*P*revious illness, *p*ast medical history
L	*L*ast meal or drink
E	*E*vents preceding injury

Box 8: First Aid Management at the Scene

Steps	Action
Step 1	Stop the burning process—remove patient from heat source
Step 2	Maintain airway—resuscitation measures may be necessary
Step 3	Assess for other injuries and check for any bleeding
Step 4	Flush chemical burns copiously with cool water
Step 5	Flush other burns with cool water to comfort
Step 6	Protect wounds from further trauma
Step 7	Provide emotional support and have someone to remain with patient to explain help is on the way
Step 8	Transport the patient as soon as possible to nearby emergency department

Emergent Phase Management

- The top priority of care is to *stop the burning process* (Box 8). During the initial first aid period at the scene, the patient must be removed from the heat source, chemicals should be brushed off and/or flushed from the skin, and the patient wrapped in a clean sheet and blanket ready for transport to the nearest hospital. Careful, local cooling of the burn wound with saline-moistened gauze can continue as long as the patient's core temperature is maintained and he/she does not become hypothermic.
  - Upon arrival at the hospital, the burned areas can be cooled further with normal saline, followed by a complete assessment of the patient and initiation of emergency treatment (Box 9). In a burn centre, the cooling may take place, using a cart shower system, in a hydrotherapy room (Fig. 9). The temperature of the water is adjusted to the patient's comfort level, but tepid is usually best, while the wounds are quickly cleaned and dressings applied.
- *Airway management* includes administration of 100% oxygen if burns are 20% body surface area or greater. Suctioning and ventilatory support may be necessary. If the patient is suspected of having or has an inhalation injury, intubation (preferably the oral route) needs to be performed quickly.
- Evidence-based procedures for the insertion of central lines and care of ventilated patients have resulted in impressive reductions in central line blood stream infection rates and

Box 9: Treatment of the Severely Burned Patient on Admission

Steps	Action
Step 1	Stop the burning process
Step 2	Establish and maintain an airway; inspect face and neck for singed nasal hair, soot in the mouth or nose, stridor or hoarseness
Step 3	Administer 100% high-flow humidified oxygen by non-rebreather mask. Be prepared to intubate if respiratory distress increases
Step 4	Establish intravenous line(s) with large bore cannula(e) and initiate fluid replacement using Lactated Ringer's solution
Step 5	Insert an indwelling urinary catheter
Step 6	Insert a nasogastric tube
Step 7	Monitor vital signs including level of consciousness and oxygen saturation
Step 8	Assess and control pain
Step 9	Gently remove clothing and jewellery
Step 10	Examine and treat other associated injuries
Step 11	Assess extremities for pulses, especially with circumferential burns
Step 12	Determine depth and extent of the burn
Step 13	Provide initial wound care—cool the burn and cover with large, dry gauze dressings
Step 14	Prepare to transport to a burn centre as soon as possible

ventilator-acquired pneumonia (VAP) [20–23].

- *Circulatory management* includes intravenous infusion of fluid to counteract the effects of hypovolemic shock for adult patients with burns >15% body surface area and children with burns >10% body surface area. Upon admission, two large bore, intravenous catheters should be inserted, preferably into, but not limited to, unburned tissue.
  - Patients who have large burns where intravenous access will be necessary for a number of days benefit from a central venous access device inserted into either the subclavian, jugular or femoral vein. The overall goal is to establish an access route that will accommodate large volumes of fluid for the first 48 h post-burn.
  - The aim of fluid resuscitation is to maintain vital organ function, while avoiding the complications of inadequate or excessive therapy. The most commonly used regimen is the Parkland (Baxter) formula: 4 ml/kg/% body surface area burn using crystalloid (Lactated Ringer's) solution (Box 10). *Fluids are calculated for the first 24 h post-burn with "0" hours being the time of the burn not the time of admission to hospital*. One-half of the 24 h total needs to be administered over the first 8 h post-burn,

Fig. 9 Cart shower for hydrotherapy

Box 10: Fluid Resuscitation Using the Parkland (Baxter) Formula

Formula	Administration	Example
4 mL lactated Ringer's solution per kg body weight per % total body surface area (TBSA) burn = total fluid requirements for the first 24 h post-burn (0 h = time of injury)	½ Total in first 8 h	For a 65 kg patient with a 40% burn injured at 1000 h:
	¼ Total in second 8 h	4 mL × 65 kg × 40% burn = 10,400 mL in first 24 h
	¼ Total in third 8 h	½ Total in first 8 h (1000–1800 h) = 5200 mL (650 mL/h)
		¼ Total in second 8 h (1800–0200 h) = 2600 mL (325 mL/h)
		¼ Total in third 8 h (0200–1000 h) = 2600 mL (325 mL/h)

N.B. Remember that the formula is only a guideline. Titrate to maintain urinary output at 30–50 mL/h, stable vital signs and adequate sensorium

while the remaining half of the estimated resuscitation volume should be administered over the next 16 h.

- It is important to remember that *the formula is only a guideline*. The infusion needs to be adjusted based on the patient's clinical response, which includes vital signs, sensorium and urinary output. For adults, 30–50 mL urine per hour is the goal and 1 mL/kg/h in children weighing less than 30 kg.
- An indwelling urinary catheter needs to be inserted at the same time as the IVs are established in order to reliably measure the adequacy of the fluid resuscitation.

- *Wound care.* Wound closure will halt or reverse the various fluid/electrolyte, metabolic and infectious processes associated with an open burn wound. The burns are gently cleansed with normal saline, if the care is being provided on a stretcher or bed. If a hydrotherapy cart shower or immersion tank is used, tepid water cleans the wounds of soot and loose debris (Fig. 10). Sterile water is not necessary.
  - Chemical burns should be flushed copiously for at least 20 min, preferably longer.
  - Tar cannot be washed off the wound. It requires numerous applications of an emulsifying agent, such as Tween 80®, Medisol®, Polysporin® ointment or mineral oil.

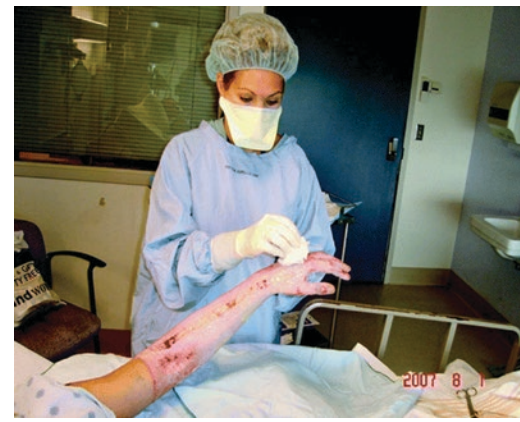

Fig. 10 Initial wound care post-admission

  - During hydrotherapy, loose, necrotic tissue (eschar) may be gently removed (debrided) using sterile scissors and forceps. Hair-bearing areas that are burned should be carefully shaved, with the exception of the eyebrows. Showering or bathing should be limited to 20 min in order to minimise patient heat loss and physical/emotional exhaustion.
  - More aggressive debridement should be reserved for the operating room, unless the patient receives conscious or deep sedation.
  - After the initial bath or shower, further decisions are made regarding wound care.

The frequency of the dressing change depends on the condition of the wound and the properties of the dressing employed. All treatment approaches have certain objectives in common (Table 6).

– Wounds are generally initially treated with a thin layer of topical antimicrobial cream. Topical coverage is selected according to the condition of the wound, desired results and properties of the topical agent (Table 7).

Table 6 Objectives of burn wound care

Objective	Rationale
Prevention of conversion	Wounds that dry out or develop an infection can become deeper. A partial-thickness wound could then convert to full-thickness and require skin grafting
Removal of devitalized tissue	Debridement, either through dressing changes or surgery, is necessary to clean the wounds and prepare for spontaneous healing or grafting
Preparation of healthy granulation tissue	Healthy tissue, free of eschar and nourished by a good blood supply, is essential for new skin formation
Minimization of systemicinfection	Eschar contains many organisms. Removal is essential in order to decrease the bacterial load and reduce the risk of burn wound infection
Completion of the autografting process	Full-thickness wounds require the application of autologous skin grafts from available donor sites
Limitation of scars and contractures	Wounds that heal well the first time tend to have fewer scars and contractures. Some degree of scar and contracture formation are, however, part of the healing process and cannot be entirely prevented

Table 7 Topical antimicrobial agents used on burn wounds

Product	Preparation	Antimicrobial action	Applications
Silver sulphadiazine (SSD®, Silvadene®, Flamazine®)	1% Water-soluble cream	Broad-spectrum antimicrobial activity	*Burn wound*: applied using the open or closed dressing method of wound care
		Poor solubility with limited diffusion into eschar	
Mafenide acetate (Sulfamylon®)	8.5% Water-soluble cream	Bacteriostatic for Gram-positive and Gram-negative organisms	*Deep partial-thickness and full-thickness burns*: applied using either the open (exposure) or closed (occlusive) dressing method
		Highly soluble and diffuses through the eschar	
	5% Solution	Same as above	*Graft site*: saturated dressings are applied
Silver nitrate	0.5% Solution	Broad-spectrum antimicrobial activity	*Burn wound or graft site*: Saturated, multilayered dressings are applied to the wound or grafted surface
		Hypotonic solution	
Petroleum and mineral oil-based antimicrobial ointments (e.g. Neosporin®, Bacitracin®, Polysporin®)	Neosporin® (neomycin, bacitracin, polymyxin B), Bacitracin® (bacitracin zinc), Polysporin® (bacitracin, polymyxin B)	Bactericidal for a variety of Gram-positive and Gram-negative organisms	*Superficial burn wound*: applied to wound in a thin (1 mm) layer and should be reapplied as needed to keep ointment in contact with wound
		Ointments have limited ability to penetrate eschar	

– Assessment criteria have been established for choosing the most appropriate agent (Box 11).
– The most commonly selected topical antimicrobial agent is silver sulphadiazine, which can be applied directly to saline-moistened gauze, placed on the wound, covered with additional dry gauze or a burn pad and secured with gauze wrap or flexible netting (Fig. 11), [24]. These dressings are changed once or twice daily.
– Cartilaginous areas, such as the nose and ears, are usually covered with mafenide acetate (Sulfamylon®), which has greater eschar penetration ability.
– Face care includes the application of warmed, saline-moistened gauze to the face for 20 min, followed by a gentle cleansing and reapplication of a thin layer of ointment, such as polymyxin B sulphate (Polysporin®) (Fig. 12).
– Silver-impregnated dressings (Acticoat®/Acticoat® Flex, AQUACEL® Ag) are also commonly used in the emergent phase of burn wound care [25]. These dressings are moistened with sterile water, placed on a burn wound and left intact anywhere from 3 to 4 days to as long as 21 days, depending on the patient's individual clinical status and particular product.
– The ideal dressing should possess particular criteria (Box 12) [26, 27]. During the first few days post-burn, wounds are examined to determine actual depth. It usually takes a few days for deep, partial-thickness wounds to "declare" themselves. Scald injuries are almost always deeper than they appear on admission and need to be closely monitored.
– Whatever topical and dressing strategies are chosen, basic aseptic wound management techniques must be followed. Personnel need to wear isolation gowns over scrub suits, masks, head covers and clean, disposable gloves to remove soiled dressings or cleanse wounds. Sterile gloves should be used when applying inner dressings or ointment to the face.

Box 11: Properties of Topical Antimicrobial Agents
- Readily available
- Pharmacologic stability
- Sensitivity to specific organisms
- Non-toxic
- Cost-effective
- Non-painful on application
- Capability of eschar penetration

Fig. 11 Applying silver sulphadiazine cream to saline-moistened gauze

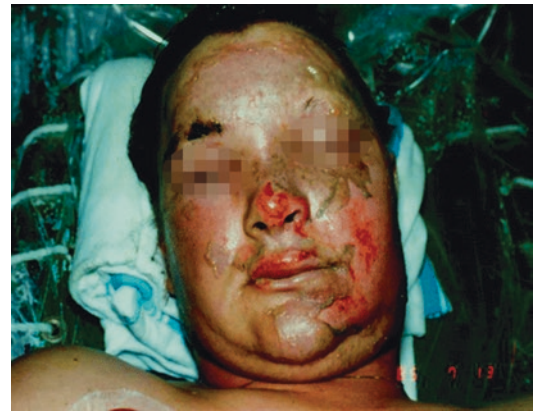

Fig. 12 Facial burn wound care

Acute Phase Priorities: closure of the burn wound, management of any complications

Box 12: Criteria for Burn Wound Coverings

- Absence of antigenicity
- Tissue compatibility
- Absence of local and systemic toxicity
- Water vapour transmission similar to normal skin
- Impermeability to exogenous microorganisms
- Rapid and sustained adherence to wound surface
- Inner surface structure that permits ingrowth of fibrovascular tissue
- Flexibility and pliability to permit conformation to irregular wound surface, elasticity to permit motion of underlying body tissue
- Resistance to linear and shear stresses
- Prevention of proliferation of wound surface flora and reduction of bacterial density of the wound
- Tensile strength to resist fragmentation and retention of membrane fragments when removed
- Biodegradability (important for "permanently" implanted membranes)
- Low cost
- Indefinite shelf life
- Minimal storage requirements and easy delivery

Acute Phase Goals of Care: spontaneous diuresis, ongoing fluid management, wound closure, detection and treatment of complications over a period of a week to many months, optimal pain management and nutrition

Acute Phase Assessment

- Fluid therapy is administered in accordance with the patient's fluid losses and medication administration.
- Wounds are examined on a daily basis, and adjustments made to the dressings applied. If a wound is full-thickness, arrangements need to be made to take the patient to the operating room for surgical excision and grafting.
- Pain and anxiety levels need to be measured and responded to on a daily basis. A variety of pharmacologic and non-pharmacologic strategies are available (Table 8) and address both the background discomfort from burn injury itself and the pain inflicted during procedural and rehabilitative activities [28–36].
- Calorie needs are assessed on a daily basis and nutrition adjusted accordingly [37–40].

Acute Phase Management

- Wound care is performed daily and treatments adjusted according to the changing condition of the wounds (Table 9). Selecting the most appropriate method to close the burn wound is by far the most important task in the acute period.

Table 8 Sample burn pain management protocol

Recovery phase	Treatment	Considerations
Critical/acute with mild to moderate pain experience	IV Morphine or Hydromorphone	Assess patient's level of pain q 1 h using VAS (0–10)
	Continuous infusion for background pain	Assess patient's response to medication and adjust as necessary
	Bolus for breakthrough or acutely painful episodes/mobilisation	Assess need for antianxiety agents
	Consider IV Fentanyl if morphine or hydromorphone are ineffective	Consider virtual reality techniques/relaxation exercises/ music distraction

(continued)

Table 8 (continued)

Recovery phase	Treatment	Considerations
Critical/acute with severe pain experience	1. IV Morphine or Hydromorphone	Consider fentanyl infusion for short-term management of severe pain
	Continuous infusion for background pain	Assess level of pain q1h using VAS (0–10) Assess patient's response to medication and adjust as necessary
	Bolus for breakthrough	Assess level of sedation using SASS score Assess need for antianxiety agents
	2. IV Fentanyl	Consider virtual reality techniques/relaxation exercises/ music distraction
	Bolus for painful dressing changes/ mobilisation	
	3. IV Versed®	
	Bolus for extremely painful dressing change/ mobilisation	
	4. Propofol Infusion	
	Consult with Department of Anaesthesia for prolonged and extremely painful procedures, i.e. major staple/dressing removal	
Later acute/rehab with mild to moderate pain experience	Oral continuous release morphine or hydromorphone—for background pain BID	Assess patient's level of pain q1h using VAS (0–10)
	Oral morphine or hydromorphone for breakthrough pain and dressing change/mobilisation	Consult equianalgesic table for conversion from IV to PO administration route Assess patient's response to medication and adjust as necessary Assess need for antianxiety agents
	Consider adjuvant analgesics such as gabapentin, ketoprofen, ibuprofen, acetaminophen	Assess for pruritus and/or neuropathic pain Consider virtual reality techniques/relaxation exercises/ music distraction

Table 9 Sample burn wound management protocol

Wound status	Treatment	Considerations
Early acute, partial or full- thickness, eschar/blisters present	Silver sulphadiazine-impregnated gauze	Apply thin layer (2–3 mm) of silver sulphadiazine to avoid excessive build-up
	Saline-moistened gauze	Monitor for local signs of infection, i.e. purulent drainage and odour, and notify M.D. re. potential need for alternative topical agents, i.e. acetic acid and mafenide acetate
	Dry gauze—outer wrap	
	Mafenide acetate (Sulfamylon®) to cartilaginous areas of face, i.e. nose, ears	
	Polymyxin B sulphate (Polysporin®) to face	
	Change BID to body, face care q4h	

Table 9 (continued)

Wound status	Treatment	Considerations
Mid-acute, partial or full- thickness, leathery or cheesy eschar remaining	Saline-moistened gauze	Saline dressings to be applied to a relatively small area due to potentially painful nature of treatment
	Dry gauze—outer wrap	Potential use of enzymatic debriding agents (Collagenase Santyl®, Elase®, Accuzyme®)
	Change BID	Monitor for local signs of infection and notify MD
	Full-thickness wounds to be excised surgically	
Late acute, clean partial-thickness wound bed	Non-adherent greasy gauze dressing (Jelonet®, Adaptic®)	Monitor for local signs of infection and notify MD
	Saline-moistened gauze	
	Dry gauze—outer wrap	
	Change once daily	
Post-op graft site	Non-adherent greasy gauze dressing (Jelonet®, Adaptic®)	Select appropriate pressure-relieving sleep surface
	Saline-moistened gauze	Monitor for local signs of infection and notify MD
	Dry gauze—outer wrap	
	Leave intact ×2 days	
	Post-op day 2, gently debulk to non-adherent gauze layer → redress once daily	
	Post-op day 5, gently debulk to grafted area	
	Redress once daily	
Early rehab, healed partial-thickness or graft site	Polymyxin B sulphate (Polysporin®) until wound stable BID	Apply thin layer (2 mm) of Polysporin® to avoid excessive build-up
	When stable, moisturising cream applied BID and prn	Avoid lanolin and mineral oil containing creams which clog epidermal pores and do not reach dry, dermal layer
Post-op donor site	(a) Hydrophilic foam dressing (i.e. Allevyn®/ Mepilex®) or (b) greasy gauze dressing (i.e. Xeroform®)	Monitor for local signs of infection and notify MD
	(a) Cover foam with transparent film dressing and pressure wrap ×24 h	
	Remove wrap and leave dressing intact until day 4 unless there is much fluid and a need to replace foam dressing earlier; if not, replace initial dressing on day 4 and leave intact until day 8. Remove and inspect status of wound healing	
	If wound unhealed, reapply a second or third foam dressing.	
	If healed, apply polymyxin B sulphate (Polysporin®) BID	
	When stable, apply moisturising cream BID and prn	
	b) Cover Xeroform® with dry gauze and secure. Leave intact for 5 days	
	Remove outer gauze on day 5 and leave open to air. Apply light layer of polymyxin B sulphate (Polysporin®) ointment. If moist, reapply gauze dressing for 2–3 more days	
	When Xeroform® dressing lifts up as donor site heals, trim excess and apply polymyxin B sulphate (Polysporin®) ointment	

(continued)

Table 9 (continued)

Wound status	Treatment	Considerations
Face	Normal saline-moistened gauze soaks applied to face ×15 min	For male patients, carefully shave beard area on admission and as necessary to avoid build-up of debris. Scalp hair may also need to be clipped carefully on admission to inspect for any burn wounds
	Remove debris gently using gauze	
	Apply thin layer of polymyxin B sulphate (Polysporin®)	
	Repeat soaks q 4–6 h	
	Apply light layer of mafenide acetate (Sulfamylon®) cream to burned ears and nose cartilage	

Table 10 Temporary and permanent skin substitutes

Biological	Biosynthetic	Synthetic
Temporary Allograft/homograft (cadaver skin) Clean, partial- and full-thickness burns Amniotic membrane Clean, partial-thickness burns Xenograft (pigskin) Clean partial- and full-thickness burns	Temporary Nylon polymer bonded to silicone membrane with collagenous porcine peptides (BioBrane®) Clean, partial-thickness burns, donor sites Calcium alginate from brown seaweed (Curasorb®, Kalginate®) Exudative wounds, donor sites Human dermal fibroblasts cultured onto BioBrane® (TransCyte®) Clean, partial-thickness burns Mesh matrix of oat beta-glucan and collagen attached to gas-permeable polymer (BGC Matrix®) Clean, partial-thickness burns, donor sites	Temporary Polyurethane and polyethylene thin film (OpSite®, Tegaderm®, Omiderm®, Bioclusive®) Composite polymeric foam (Allevyn®, Mepilex®, Curafoam®, Lyofoam®) Clean, partial-thickness burns, donor sites Non-adherent gauze (Jelonet®, Xeroform®, Adaptic®) Clean partial-thickness burns, skin grafts, donor sites
Semi-permanent Mixed allograft seeded onto widely meshed autograft Clean, full-thickness burns	Semi-permanent Bilaminar membrane of bovine collagen and glycosaminoglycan attached to silastic layer (Integra®) Clean, full-thickness burns	
Permanent Cultured epithelial autografts (CEA) grown from patient's own keratinocytes (Epicel®) Clean, full-thickness burns Allograft dermis decellularized, freeze-dried and covered with thin autograft or cultured keratinocytes (AlloDerm®) Clean, full-thickness burns		

During the dressing changes, nurses debride small amounts of loose tissue for a short period of time, ensuring that the patient receives adequate analgesia and sedation. As the devitalized burn tissue (eschar) is removed from the areas of partial-thickness burn, the type of dressing selected is based on its ability to promote moist wound healing. There are biologic, biosynthetic and synthetic dressings and skin substitutes available today (Table 10). Areas of full-thick-

ness damage require surgical excision and skin grafting. There are specific dressings appropriate for grafted areas and donor sites [41–47].
- Ongoing rehabilitation, offered through physiotherapy and occupational therapy, is an important part of a patient's daily plan of care [48, 49]. Depending on the patient's particular needs and stage of recovery, there are certain range-of-motion exercises, ambulation activities, chest physiotherapy, stretching and splinting routines to follow [50–52]. The programme is adjusted on a daily/weekly basis as the patient makes progress towards particular goals and as his/her clinical condition improves or worsens.

Rehabilitative Phase Priorities: maintaining wound closure, scar management, rebuilding strength, transitioning to a rehabilitation facility and/or home.

Rehabilitative Phase Goal of Care: returning the burn survivor to a state of optimal physical and psychosocial functioning.

Rehabilitation Phase Assessment
- The clinical focus in on ensuring all open wounds eventually close, observing and responding to the development of scars and contractures and ensuring that there is a plan for future reconstructive surgical care, if the need exists.

Rehabilitation Phase Management
- Wound care is generally fairly simple at this time. Dressings should be minimal or non-existent. The healed skin is still quite fragile and can break down with very little provocation, which can be very frustrating for patients. The need to moisturise the skin with water-based creams is emphasised in order to keep the skin supple and to decrease the itchiness that may be present, which is another frustrating sequelae during this phase of recovery [53–56].
- Visits to outpatient burn clinic provide opportunities for ongoing contact between staff, patients and family post-discharge, wound evaluation and assessment of physical and psychological recovery.
- Scar maturation begins and contractures may worsen. Scar management techniques, including pressure garments, inserts, massage and stretching exercises, need to be taught to patients, and their importance reinforced with each and every visit [57–65].
- Encouragement is also essential in order to keep patients and families motivated, particularly during the times when progress is slow and there seems to be no end in sight to the months of therapy [66, 67].
- The burn surgeon can also plan future reconstructive surgeries for the patient, taking into consideration what improvements the burn patient wishes to see first.

5.2 Surgical Care

- Full-thickness burn wounds do not have sufficient numbers of skin-reproducing cells in the epidermal appendages to satisfactorily heal on their own. Surgical closure is needed.
- Common practice in surgical burn management is to begin surgically removing (excising) full-thickness burn wounds within a week of admission. Larger areas of burn are generally removed (i.e. thorax/back/arms/legs) before smaller areas (face/hands/feet) in order to reduce the bacterial load. Most patients undergo excision of non-viable tissue (Fig. 13) and grafting in the same operative procedure. In some instances, if there is concern the

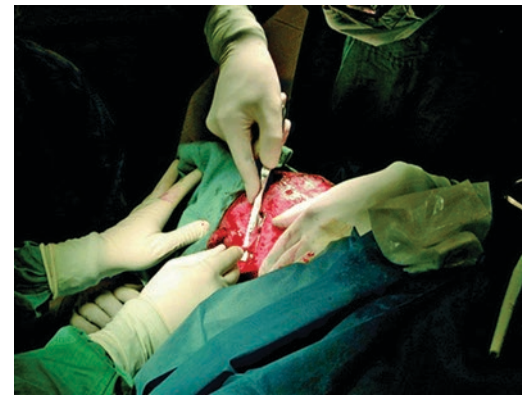

Fig. 13 Surgical excision of full-thickness burn wound

wound bed may not be ready for a graft, the burn wounds are excised and then covered with topical antimicrobials and/or followed by a temporary biologic or synthetic dressing.

- If alert pre-operatively, patient preparation includes educational and psychological support to ensure an optimal recovery period.
- The donor skin (skin graft), which is harvested but not applied in this first O.R., using a dermatome (Fig. 14), is then wrapped up in sterile fashion and placed in a skin fridge for later application. Allograft (cadaver skin) may be laid down temporarily on the excised, recipient bed area, providing skin-like properties.
- Two days later, the patient returns to the OR to have the excised wounds (recipient bed) examined and the donor skin laid as a skin graft on the clean recipient bed. Dressings remain intact for 5 days postoperatively.
- Concern over blood loss and lack of sufficient donor sites are the two limiting factors when attempting to excise and graft patients with extensive wounds.
- Grafts can be split-thickness or full-thickness in depth, meshed or unmeshed in appearance and temporary or permanent in nature (Table 11).
- Grafts should be left as unmeshed sheets for application to highly visible areas, such as the face, neck or back of the hand (Fig. 15).
- Sheet grafts are generally left open and frequently observed by nursing and medical staff for evidence of serosanguinous exudate under the skin.
- On other parts of the body, grafts can be meshed using a dermatome mesher (Fig. 16). The mesher is set to an expansion ratio chosen by the surgeon. An expansion ratio of 1.5:1 allows for exudate to come through and be wicked into a protective dressing, while at the same time be cosmetically acceptable (Fig. 17). Wider expansion ratios (3:1, 6:1) allow for increased coverage when there are limited donor sites available.
- Meshed skin grafts are generally covered with one of a number of possible options, including silver-impregnated, vacuum-assisted closure, greasy gauze or cotton gauze dressings. Most are left intact for 5 days to allow for good

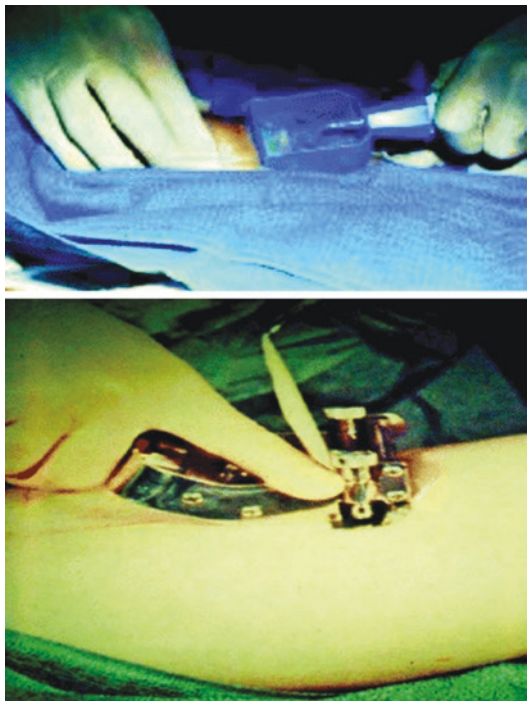

Fig. 14 Harvesting a split-thickness skin graft. Adrenalin/saline soaks may be applied to donor sites to control bleeding before the donor dressing is applied. Tumescence and electrocautery may also be used

Table 11 Sources of skin grafts

Type	Source	Coverage
Autograft	Patient's own skin	Permanent
Isograft	Identical twin's skin	Permanent
Allograft/homograft	Cadaver skin	Temporary
Xenograft/heterograft	Pigskin, amnion	Temporary

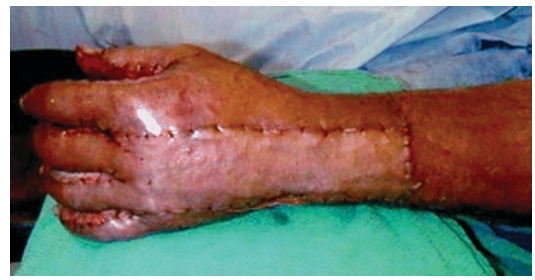

Fig. 15 Unmeshed split-thickness sheet graft

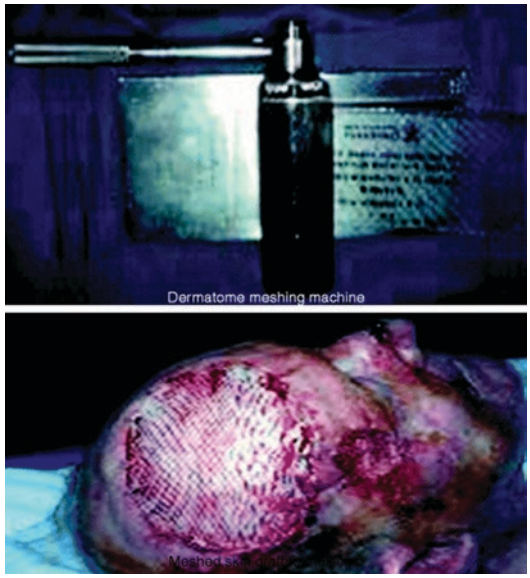

Fig. 16 Putting a skin graft through a dermatome mesher. Once harvested, graft is placed on a plastic dermatome carrier and run through a meshing machine. Mesh ratio pattern from 1.5:1 (most common) to 12:1. If donor sites are few and area to cover is large, meshing ratio will increase to 3:1 or 6:1. Exudate can come up through the holes in the mesh pattern to be wicked into the intact dressing. Grafts to the face and hands are not meshed for optimal cosmetic results. These sheet grafts are nursed open

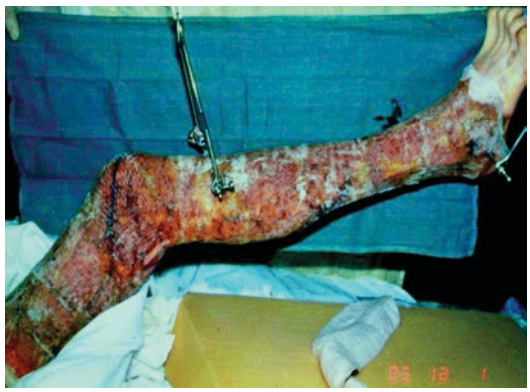

Fig. 17 Meshed split-thickness skin graft

vascularisation between the recipient bed and the skin graft.

- Following the initial "take down" at post-op day 5, the dressings are changed every day until the graft has become adherent and stable, usually around day 8.
- For the next year or so post-burn, the skin grafts mature and their appearance improves (Fig. 18). Patients are cautioned that the skin graft appearance will "mature" over the next year and not to be overly concerned about the post-operative appearance.
- The donor site can be dressed with either a transparent occlusive, hydrophilic foam or greasy gauze dressing (Fig. 19). Donor sites generally heal in 10–14 days and can be reharvested, if necessary, at subsequent operative procedures (Fig. 20). Patients should be provided with adequate pain management and support as donor sites are more painful than grafted sites and, for many patients, more painful than the initial burn injury.
- Over the past 10 years, there have been major advancements in the development, manufacture and clinical application of a number of temporary and permanent biologic skin substitutes. Most of these products were initially developed in response to the problems faced when grafting the massive (i.e., >70%) burn wound where donor sites are limited (Table 12). The search for a permanent skin substitute continues.

5.3 Pharmacological Support

Burn patients are assessed for:

- Tetanus toxoid, because of the risk of anaerobic burn wound contamination. Tetanus immunoglobulin is given to those patients who have not been actively immunised within the previous 10 years.
- Pain medication, which should always be administered intravenously during the hypovolemic shock phase as gastrointestinal function is impaired and intramuscular (IM) medications would not be absorbed adequately.
  - The medication of choice for moderate to severe pain management is an opioid, such as morphine or hydromorphone, as they can be given intravenously and orally and are available in fast-acting and slow-release forms (Table 8).

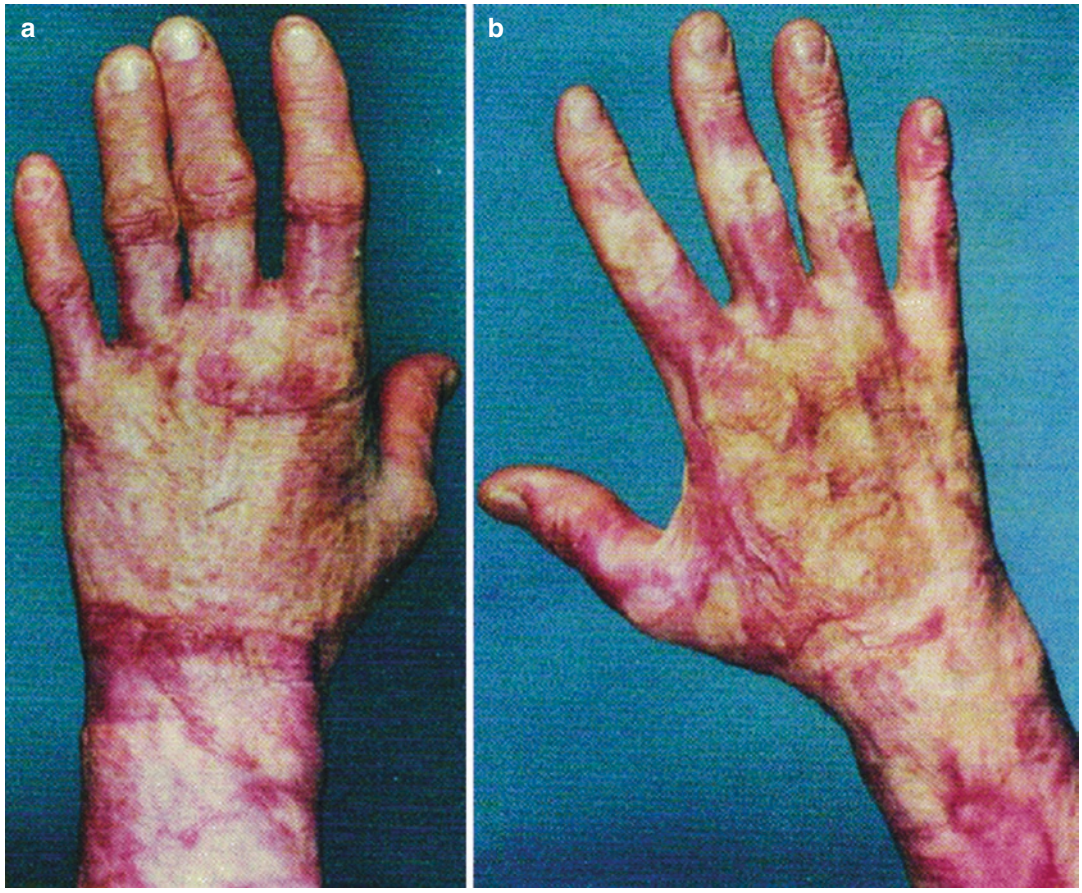

Fig. 18 (**a**, **b**) Mature split-thickness skin graft

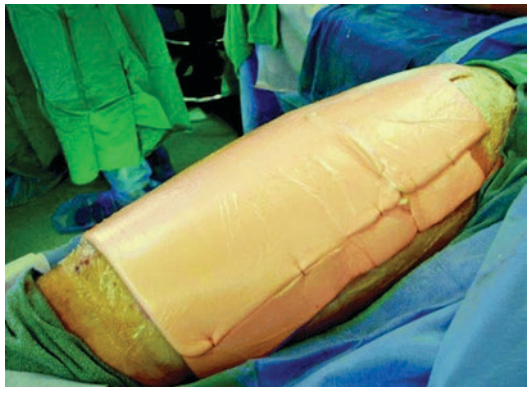

Fig. 19 Harvested donor site

Fig. 20 Healed donor site

Table 12 Biologic skin replacements

Source	Product	Description
Cultured epithelial autograft (CEA)	Epicel® (Genzyme Corporation, Massachusetts)	Cultured, autologous keratinocytes grown from patient's donated skin cells
		6–8 cells thick, 2–3 weeks culture time
		Lacks dermal component; susceptible to infection
		Lacks epidermal cell-to-connective tissue attachment and is, therefore, very fragile
Dermal replacement	Integra® (Johnson & Johnson, Texas)	Synthetic, dermal substitute
		Neodermis formed by fibrovascular ingrowth of wound bed into 2 mm thick glycosaminoglycan matrix dermal analogue
		Epidermal component, silastic, removed in 2–3 weeks and replaced with ultrathin autograft
		Functional burn wound cover
		Requires 2 O.R.s: 1 for dermal placement, 1 for epidermal graft
Dermal replacement	AlloDerm® (LifeCell Corporation, Texas)	Cadaver allograft dermis rendered acellular and nonimmunogenic
		Covered with autograft in same O.R. procedure

Table 13 Anxiolytics commonly used in burn care

Generalised anxiety	Situational anxiety (dressing changes, major procedures)	Delirium
Lorazepam (Ativan®) IV	Midazolam (Versed®) IV	Haloperidol (Haldol®) IV
Works nicely in combination with analgesics for routine dressing changes and care	Works nicely in combination with analgesics when very painful and prolonged procedures are performed	Works nicely for patients who appear agitated or disoriented

  - As the burn wounds close and the patient's pain level increases, reductions in analgesic therapy should occur by careful taper, rather than abrupt discontinuation, of opioids.
- Sedative agents (Table 13).
- Non-pharmacologic approaches to pain management (hypnosis, relaxation, imagery).
- Topical antimicrobial therapy for burn wound care (Table 7).
  - The most widely used broad-spectrum antimicrobial agent is silver sulphadiazine. Local application on the burn wound is necessary, as systemic antibiotics would not be able to reach the avascular burn wound.
  - Mafenide acetate is indicated for burned ears and noses as it has a greater ability to penetrate through cartilage.

Table 14 Medications commonly used in burn care

Types and names	Rationale
Gastrointestinal care	
Ranitidine (Zantac®)	Decreases incidence of stress (Curling's) ulcers
Nystatin (Mycostatin®)	Prevents overgrowth of *Candida albicans* in oral mucosa
Milk of magnesia, lactulose, docusate sodium, sennosides, glycerin, or bisacodyl suppository	Prevents/corrects opioid-induced constipation
Nutritional care	
Vitamins A, C, E, and multivitamins	Promotes wound healing, immune function
Minerals: selenium, zinc sulphate, iron (ferrous gluconate and sulphate), folic acid, thiamine	haemoglobin formation and cellular integrity

- Systemic antibiotics when a burn wound infection has been clinically diagnosed or other indicators of sepsis are present, such as pneumonia or uncontrolled fever.
- Additional medications to manage gastrointestinal complications treat antibiotic-induced superinfections and boost the patient's metabolic and nutritional status (Table 14).

5.4 Psychosocial Support

Emotional and psychological support to burn survivors is an essential part of their ongoing care, especially in the later phase of recovery when the focus can shift from survival and wound healing, to navigating a future that might appear quite different from the one that the patient had envisioned. Nurses can provide patients with opportunities to verbalise their feelings in a non-judgemental atmosphere. Discussing and acknowledging fears and anxieties is an important first step in overcoming them [68–72]. Caring attention to significant family and friends provides them with necessary support so they, in turn, can serve as the patient's single most important social support [73, 74].

Some burn patients were troubled psychologically pre-burn. They may have formal psychiatric diagnoses and/or histories of drug and/or alcohol abuse. For others, the psychological trauma begins with the burn injury. Referral to a psychiatrist or psychologist for supportive psychotherapy and/or medication can make a positive difference in those situations, where patients may be identified as experiencing acute stress disorder or post-traumatic stress disorder [75, 76]. It is important, however, before such referrals are made, to discuss the situation with the patient (if he/she is considered mentally competent). This disclosure provides the team with an opportunity to share their interpretation of the patient's behaviours and to listen to how the patient views his/her coping abilities and behaviours. The burn patient and his family need to feel supported and not stigmatised by the recommendation to seek psychological support. More recently, post-traumatic growth has been identified in the burn patient population, where improvements in particular life domains have been found to exceed pre-burn levels and patients declare their life is better after the burn injury than it was before [77].

The unique and invaluable role of patient and family support groups has been examined and encouraged by burn team members [78–84]. The power of the lived experience is profound. The advice and caring that comes from one who truly knows what it is like to survive a burn injury or the family member of one who has been burned is valuable beyond measure. Many burn centres are fortunate to have a burn survivor support group affiliated with them. Based in the USA, but with members from around the world, the Phoenix Society has hundreds of area coordinators and volunteers, through the SOAR (Survivors Offering Assistance in Recovery), who meet with burn survivors in their communities and help; however, they can visit http://www.phoenix-society.org or email info@phoenix-society.org or call 1-800-888-2876 (BURN). Work/school re-entry programmes and burn camps have also been identified as valuable adjuncts to ongoing, community-based care [85–88].

5.5 Professional Burn Nursing

Working among the burned can offer burn nurses and all burn team members an invaluable opportunity, both personally and professionally [89, 90]. Efforts to continually improve the care provided to this most challenging of patient populations, within current health care systems, is ongoing [91–93].

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Rehabilitation and Therapy of the Burn Patient

Matthew Godleski and Miranda L. Yelvington

1 Burn Rehabilitation

The overarching goals of burn rehabilitation are the restoration of function, independence, and quality of life following burn injury. Reaching this goal requires a detailed understanding of burn injury and wound care, interventions to manage short- and long-term complications such as contracture and scar hypertrophy, and the ability to translate care plans through phases of care including community re-entry and psychological well-being [1, 2]. The following chapter summarizes key elements of burn rehabilitation and management strategies.

2 Patient Assessment and Care Plan Development

For any significant burn injury, early assessments should incorporate a functional history that includes an understanding of the patient's baseline activities and any pre-existing medical conditions that altered function, their social background and roles, and patient-specific goals and concerns. Ongoing treatment should consider these goals and background as the plan of care is determined and should be mindful of the potential psychological impact and quality of life as well as the patient's peer support. Concomitant injuries may also be present, particularly for instances of trauma.

Specific to the burn injury itself, multiple factors should be considered. Characteristics such as burn size (total body surface area), depth and location of injury, inhalational injury, and pre-existing medical conditions can predict hospital length of stay, surgical needs, and associated general immobility from hospitalization [3–5]. Typically, superficial and superficial partial thickness burn injuries will heal spontaneously and do not have the same concerns associated with deeper injuries. However, pain and edema often still require management to aid in short-term functional recovery. Most of the consequences detailed within this chapter are specific to deep partial and full-thickness burn injuries in which the body's capacity to heal spontaneously is compromised, skin grafting is frequently necessary, and more profound scarring and metabolic changes are triggered [6]. The location of burn injury must also be considered—particularly for areas of high function such as the hands and face and skin approximating bony joints.

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Finally, the source of burn injury can play a role in anticipated rehabilitation needs, particularly in the case of electrical injuries.

Burn injury-associated impairments are somewhat unusual in their time course compared to other traumatic injuries. Key issues such as edema, contracture, and hypertrophy can be successfully treated or prevented, but are also recurrent due to the ongoing healing process and require sustained treatment efforts to avoid progressive development of scarring complications [7, 8]. As a result, treatment programs must consider daily goals as well as long-term outcomes to decrease the risk of relapses throughout the scar maturation phase. This often requires therapy, home exercise programs, and scar management modalities during all phases of care (intensive care, acute care and rehabilitation, ambulatory care) that are tailored to patient status and needs across the spectrum of recovery. Finally, to be successful these approaches will also often need to be coordinated with pain control methods and consideration around potential psychological adjustment or distress.

3 Contracture

Contracture is defined as a loss of range of motion (ROM) or malalignment of anatomical structures such as joints due to the development of scar tissue and the loss of normal soft tissue length and extensibility. By convention, contracture in burn injury is referred to by the direction of resistance; for example, an elbow flexion contracture impairs elbow extension [9].

Contracture is a common complication of burn injury and is associated with normal processes of healing, wound contracture, and scarring leading to a loss of normal skin elasticity [7]. Despite prevention as part of the standard of care, contracture is frequently present at the time of acute care discharge, with a reported incidence of 38.7% incidence for shoulder, elbow, hip, and knee contractures [10]. Incidence is related to factors such as length of stay, skin grafting, size and distribution of burn injury while the severity of contracture was associated with graft size, amputation, and presence of inhalational injury. Mean losses of normal range of motion typically range from 20° to 65° depending on the joint involved, reflecting an 18–45% loss of the normal arc of movement [11].

The potential impact of contracture must consider not only skin overlying joints, but also in adjacent regions. Full joint motion requires mobility and flexibility of a larger pool of soft tissue described as cutaneous functional units (CFUs) [12]. These pools of soft tissue are shared such that adjacent joints (e.g., elbow and shoulder) may mobilize the same areas of skin during full joint motion. Following burn injury, this pliable skin is replaced with scar tissue with reduced elasticity. The extent of CFU involvement has been correlated to ROM outcomes [13, 14].

In burn recovery, ROM is measured primarily through goniometry, though additional tools have been validated for thumb opposition and compound finger flexion that facilitate tracking the movement of smaller joints less amenable to goniometry use [15, 16]. Revised goniometric techniques that better consider the impact of burn scar contracture are newly available and should be considered in current clinical care [14] (Fig. 1). Joint mobility should be assessed not only for individual joint movements but also for composite movements of multiple joints that may exhaust the shared length and elasticity of the required tissue.

The formation of burn scar contractures can be physically limiting as well as cosmetically altering. Scar bands, webbing between digits, microstomia (loss of opening volume of the mouth), ectropion (inversion of the eye lid), and lagophthalmos (incomplete eyelid closure) are

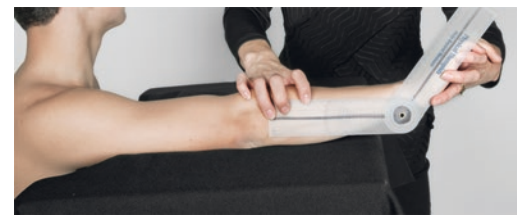

Fig. 1 A revised goniometric technique for measuring wrist extension that incorporates the potential impact of abnormal skin movement on joint range of motion. Photo credit: Ingrid Parry

common complications of severe burn injuries and can have a direct impact on a burn survivors quality of life [6, 17].

Contracture prevention requires a dynamic approach that must be modified as the patient moves through wound healing and scar maturation. Early interventions such as positioning and orthosis use are frequently used in the acute care setting. These modalities can be more difficult to employ for prolonged periods of time as patients improve in level of consciousness, mobility, and independence, while treatments such as active stretching, strengthening, and activities of daily living are benefited by increased patient strength and wakeful compliance.

3.1 Mobilization

Early mobilization is key to limit the impact of bed rest, reduce adverse events such as pressure injuries, and to begin the process of functional recovery and contracture prevention [18, 19]. Specific to the post-grafting period, mobilization must balance concerns for early graft loss with the areas above. In many cases, surgeons will require a period of immobilization prior to resuming activity. Early post-operative mobilization has been proposed, but medical literature to guide-specific decision-making is limited. Recent practice guidelines have been proposed from the burn rehabilitation community regarding early ambulation for patients with smaller grafts (less than 300 cm^2) which are not overlying joints and that can be effectively braced and have pressure dressings applied and can serve as a starting point for team decisions regarding early post-operative therapy.

3.2 Positioning

Patient positioning with or without the use of positioning devices can be an important tool in the prevention of contracture during the acute phase of care [20]. The body area affected by the burn should be positioned opposite the direction of potential burn scar contracture. Positioning must also consider the expected "position of comfort" in a setting of trauma and pain—most often the fetal position—as well as the impact of immobility and bed rest. Practice guidelines exist to serve as an effective starting point for considering positioning, though individual scenarios and injury patterns should be considered in all cases for specific prescriptions of care.

3.3 Orthosis Use

Orthoses are frequently used to provide prolonged anti-contracture positioning and low-load stretching, particularly during periods of early graft fragility and reduced level of consciousness and can have focused application in later care (Fig. 2). A large range of orthoses have been employed in burn recovery to prevent and treat losses in ROM through prolonged, passive stretching, though scientific data supporting use of specific designs is limited, as are outcomes studies evaluating specific approaches and prescriptions of use [21–23]. While there are theoretical concerns regarding the influence of prolonged stretch on the development of contracture during wound healing, recent analyses have found substantially decreased odds ratios of developing contracture through orthotic usage as a therapy tool [24, 25].

Fig. 2 An example of a hand and wrist orthosis used to prevent contracture and reduce edema during the acute phase of care. Photo credit: Miranda Yelvington

3.4 Stretching

Mechanical stretching and massage of scar tissue to improve extensibility are also traditional approaches to burn-associated contracture. Like other interventions, specific medical literature to guide technique and outcomes are limited but suggest benefit for burn recovery [26, 27]. Stretching has the theoretical advantages of being focused on specific areas of ROM losses, progressive throughout a treatment to continually advance ROM gains, and can be integrated into functional or recreational activities over time. Stretching protocols should be designed specifically for each patient and be based on the CFU and joint involvement.

3.5 Scar Massage

Scar massage is typically deferred immediately following skin grafting to prevent early graft shearing or superficial injury, but a number of techniques exist as potential tools once skin resilience has improved. However, data is lacking regarding the impact of massage on burn scar, and a recent randomized, controlled trial failed to demonstrate any significant, long-term benefits to scar characteristics such as elasticity, erythema, or scar thickness [28].

3.6 Functional Impact of Contracture

The specific functional impairment from contracture remains a complex issue. At face value, the basic relationship is simple—as ROM decreases, impairment is expected to increase. However, injuries of some locations on the body (e.g., hands) have much larger functional implications than a simple size and depth of burn for another location (e.g., torso). Predicting the impact of specific contractures is also challenged by the potential for multi-joint ROM losses leading to compound movement issues [29]. Finally, the functional needs of individual patients and baseline ROM may also vary.

Contractures affecting major joints can directly impact performance of activities of daily living (ADL). Often patients with contractures develop compensatory strategies which allow functional activity performance but may put additional stresses on less affected joints. Therapy evaluation to assess a patient's ADL performance is recommended if functionally limiting contractures are present.

4 Edema

Inflammation and wound healing lead to formation of edema particularly in the acute phase of care [30]. Functionally, this can hinder mobility and cause pain particularly in dependent areas and can factor into contracture. Elevation of dependent limbs above the heart can reduce edema and can be initiated early post-injury, and edema in the head and face can be managed by elevating the head of the bed. Compressive and positioning orthoses can reduce edema while preventing contracture and become increasingly important for the lower extremities as patients mobilize. Edema can be particularly limiting in the setting of hand injuries, and early graded pressure approaches can improve pain and ROM, including the use of self-adherent elastic wraps [31] (Fig. 3). With further healing and resolution of wound dressings compression gloves can be employed. Active muscle contraction and functional use of the hand should be encouraged to

Fig. 3 An example of the use of self-adherent elastic wraps for post-burn edema management. Photo credit: Miranda Yelvington

promote edema mobilization. When monitored over time, a figure-of-eight measurement technique has been found to be reliable and valid for hand edema in the burn patient population [32].

5 Scar Hypertrophy

Scar formation is common following burn injury and is associated with many factors ranging from depth of injury, complications, age, and genetic background [33]. In many cases, scarring becomes hypertrophic, with progressive increases in scar height and thickness, altered pigmentation, erythema, and reduced pliability. Multiple measurement tools are available, with the Vancouver Scar Scale being one of the most commonly used. Serial measurements may be challenging due to the slow rate of change and the need to establish reproducible locations for measurement particularly in the setting of larger burn injuries [34–36].

The two primary means of treatment are pressure garments and the use of insert materials (silicone or non-silicone gels and sheets). Pressure garments influence the collagen remodeling phase of wound healing. While the exact mechanism of action is unknown, it may be related to impact on local hydration, circulation, or inflammation [37, 38]. Recent reviews of the available medical literature have found that pressure therapy is effective for scar height and erythema, less clearly associated with improvements in scar pliability and joint range of motion, and less likely to impact pigmentation or scar maturation. Garments should typically be used for wounds taking longer than 14–21 days to heal and for all skin grafts [8]. Pressure garments should be employed as soon as wound healing allows application without adverse effect on dressings or injury from shearing, and worn 23 hours per day for 12 months or until scar is mature. Garments should optimally be custom fit to achieve 20–30 mmHg of pressure and should be replaced every 2–3 months as needed [8]. Custom garments can be cost prohibitive for some patients. Many prefabricated pressure garment options are now available but have not been extensively compared to the results obtained from custom garments.

Insert materials such as silicone and non-silicone gels, gel sheets, elastomers, or neoprene can benefit problematic, immature burn scars which may not respond to pressure garment therapy alone [39]. Silicone has been hypothesized to mitigate hypertrophy through mechanisms such as occlusion and hydration of the skin [39, 40]. Recent practice guidelines for the use of silicone gels and sheets have noted no clear benefit to silicone versus non-silicone products and noted that silicone gels may have reduced adverse reactions compared to gel sheets [40]. Inserts should be applied in cases likely to form hypertrophy scars once the wound has re-epithelialized.

6 Skin Physiology Following Burn Injury

The skin is the largest organ in the human body, and it plays a range of physiological roles including the sense of touch, temperature regulation, and moisturization of the skin. The majority of these functions occur through dermis-derived structures that are compromised with deep tissue injury and which typically remain impaired despite split thickness or sheet grafting. Long-term physiological skin changes from deep dermal injury should be considered in early recovery and patient education as they frequently persist and can have lasting functional consequences [41].

The loss of distal nerve endings in the dermis leads to an increased threshold for detecting light touch, cold, and heat and a subsequent loss of perceived skin sensation and these changes typically persist long term [41, 42]. Temperature regulation occurs through the skin through vascular shunting of blood via vasodilation and constriction as well as sweating and piloerection. Following skin grafting, these processes remain impaired with consequent decreased heat and cold tolerance relative to the size of skin injured though heat acclimation exercises may improve heat tolerance over time [42–44]. This is of particular importance given the benefits of strength training and aerobic conditioning in burn recovery [45].

Superficially, the loss of sebaceous glands and oil production may seem trivial, but problems with pruritus, dry skin, and need for artificial lubrication through lotion remain some of the most common long-term complaints following major burn injury [41]. Beyond the need for early education, alterations in skin oil may need to be considered for activities and employment that are accompanied by exposure to chemical irritants, dry heat, or cleaning materials.

7 Burn-Specific Complications

7.1 Peripheral Nerve Injury

The incidence of peripheral nerve injury in burn injury ranges widely in the medical literature depending on the inclusion criteria regarding the severity of burn injury [46, 47]. In those categorized as major burn injury, research has found an incidence of 11% and associations with larger burns, more days on mechanical ventilation, increased surgical requirements, and longer periods of hospitalization [46].

Focal peripheral nerve injury typically occurs local to deep burn injury, but can also arise as a consequence of other features of burn injury such as critical illness, pressure from positioning or dressings, edema, or compartment syndrome. Focal injury incidence typically follows that of entrapment neuropathies, with the median, ulnar, and peroneal nerves most often at risk and the upper extremity a more common site than the lower [46–48].

7.2 Heterotopic Ossification

Heterotopic ossification is the formation of pathological, ectopic bone in soft tissue, and it is associated with a wide range of conditions ranging from spinal cord injury and traumatic brain injury to bony fractures and joint replacement surgeries. In the setting of burn, it is a rare complication associated with larger total body surface area of injury, and most often occurring adjacent to the elbow joint [49]. While rare, the rehabilitation implications of heterotopic ossification can be severe, with patients experiencing increased pain, loss of ROM, and nerve entrapment particularly involving the ulnar nerve [50]. These changes may often be first noted during therapy interventions. Described medical interventions for prevention and treatment have included non-steroidal anti-inflammatory drugs, bisphosphonates, and radiation, and many patients require surgical resection of heterotopic ossification once the process has matured and the risk of recurrence has diminished months after onset.

Specific rehabilitation guidelines for treating heterotopic ossification are limited. Early studies and scientific theories raised concerns that early, aggressive mobilization may be associated with the development and progression of heterotopic ossification [51]. However, these concerns have not been clearly substantiated in clinical studies and prolonged immobilization has also been implicated in risk of developing heterotopic ossification. In addition, avoiding early range of motion in the at-risk population would often lead to significant soft tissue contracture and loss of function. In cases where heterotopic ossification does develop, surgical interventions must often be delayed for months post-injury. This leaves therapy and range of motion as some of the few interventions available to restore function in early phases, and there is limited evidence that they may improve outcomes. While questions remain to the exact role of therapy relative to heterotopic ossification, it has been suggested that immobilization should be limited and passive and active range of motion should continue based on the currently available scientific literature [51–53].

7.3 Electrical

Electrical injuries can cause all of the complications and therapy concerns discussed in this chapter, but due to the potential for deep tissue injury from electrical current traveling through the body can cause a wide range of additional pathology with functional implications. Electrical injury is associated with four-fold increased risk

of peripheral nerve injury, spinal cord injury and dysfunction, increased rates of limb amputation, ophthalmological complications including cataract formation, and a wide range of neurological and psychological manifestations [46, 54–58].

Complicating these issues is the fact that in many cases development of complications can continue to progress for weeks or months following injury. This may be due to the varied nature of the injury itself, with trauma occurring not only from thermal energy, but also due to vascular injury and pathological changes at a cellular or subcellular level [46, 59], such as lasting cell membrane damage and protein denaturation. In addition—and likely also due to the unusual nature of damage from electrical injury—routine medical testing may fail to identify focal pathology [60]. As a result, rehabilitation providers should have a low index of suspicion for electrical injury-associated complications both at onset and over time, and consider the wide range of potential areas of tissue injury when reviewing patient complaints.

8 Quality of Life, Psychological, and Social Considerations

Quality of life and restoration of prior life function will be the goal for the majority of patients with burn, though substantial barriers may be in present [41, 61, 62]. Within this goal, rehabilitation providers need to be considerate of psychosocial aspects of recovery and care as well as insuring that functional goals translate to restoration of pre-injury roles and activities. As an example, return to work can be a complex goal requiring consideration of a host of physical and psychological outcomes [63–65].

The psychological needs of patients often evolve over time and through transitions in care [66]. Beyond burn size, factors such as age and gender can be predictors of physical, mental health outcomes, and perceptions of body image [67, 68]. Post-traumatic stress disorder can be common post-burn injury and should be subject to screening [69, 70]. Post-discharge, patients may be at increased risk of urgent mental health care needs [71]. As a result, rehabilitation care plans should also consider use of resources such as peer support, inclusion and education of social supports, and multidisciplinary care teams to help insure the best functional outcomes and quality of life for burn survivors.

9 Conclusions

Burn injuries can lead to a sequela of events that can complicate the rehabilitation course. Hypertrophic scars, contracture formation, loss of lean body mass and the ill effects of prolonged immobilization all complicate the recovery process. Early and aggressive occupational and physical therapy, a structured orthosis and positioning program, edema and scar management are all factors that can combine to promote optimal outcomes for burn survivors. Further research into burn-specific considerations such as CFUs, scar management, and the effect of multi-joint contractures will continue to shape the future of burn rehabilitation.

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Mental Health in Burn Survivors

Nicolas Bergeron, Suzie Bond, and Matthew Boyle

1 Introduction

Worldwide, there has been an overall trend towards a decreased incidence of burns as well as reduction in their severity. This has often lead to decreased lengths of stay and reduced mortality from burns [1]. This positive trend is likely secondary to the prevention programs developed and the astounding advances made with regard to treatment. Albeit, achievements in public health and surgical procedures have led to the establishment of new challenges in terms of rehabilitation and social reintegration.

A significant number of survivors, in fact, experience difficulties adapting and are ultimately affected by one or more disabling mental health disorders [2]. The disabilities ensuing from burns, in addition to disfigurement, often bring about stigmatization and social exclusion. The research conducted on the quality of life of major burn survivors over the medium and long term is quite telling, with serious injuries and psychological issues being the two most significant factors [3–5]. Mental health conditions in burn survivors can be associated with longer lengths of stay in hospital and worse medical outcomes such as increased burn wound infections, nutritional deficiencies, and skin graft failures [6].

The psychological issues associated with major burns are frequent, complex and varied, and go well beyond post-traumatic stress disorder (PTSD) [7]. For this reason, burn survivors need personalized mental health care from the moment they are admitted to the care unit until their reintegration into the community [8]. Therefore, addressing the often complex mental health needs of burn survivors is imperative in managing their pathway towards recovery. Integration of caregivers specialized in mental health on the burn health care team is another key element to optimize their recovery.

This chapter aims to identify the primary psychiatric and psychological issues touching burn survivors as well as the mental health interventions that can help facilitate the recovery of burn survivors and their loved ones.

2 Profile of Burn Victims

The majority (70%) of major burn survivors in developed countries are men [9]. It has been suggested that this may be due to the fact that men

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are more likely to take part in risk-taking behaviors than their female counterparts [9, 10] and over-representation in high-risk positions (e.g., roofers, electricians, machinists in the chemical industry).

In addition to risk-taking and hazardous jobs, there are also cases where a person's skills or judgment are compromised, such as when they drink alcohol or use drugs [11, 12]. One-third of the persons admitted to burn units are either under the influence or suspected to have been under the influence (of drugs or alcohol) at the time of the event [13, 14]. Moreover, the instances of major burns associated with drinking are on the rise [15]. In the United States, the number of patients admitted for major burns who tested positive for cannabis grew substantially over the last decade, from 6% in 2002 to 27% in 2011 [16].

One-third of major burn survivors present with premorbid mental problems that may affect cognitive processes such as attention and judgment or are linked to impulsive behaviors, and therefore increase the risk of injury [12, 13, 17]. While self-immolation is generally seen to constitute an extreme means of political protest, persons who set themselves on fire, whether or not they are suicidal, also generally suffer from a mental health disorder [18, 19]. A recent study done in Ontario showed that there was an increase in the rates of mental health visits to the emergency room in the 12 weeks prior to a burn injury, indicating the importance of addressing mental health needs as a possible public health preventative measure for burns [20].

A burn injury can also occur when a person's state of awareness is compromised due to another medical issue such as epilepsy or diabetic hypoglycemia. Also, persons whose reaction time is diminished due to a loss of mobility (e.g., paralysis, advanced age) have a higher risk of suffering burns. In regions with extremely cold seasons, the homeless, the mentally ill or persons who are intoxicated will often experience frostbite [21].

It appears that major burns are more likely to occur among the most vulnerable members of the population, as well as those in a socially precarious situation (e.g., persons with little or no education, the unemployed or those with a low income, single mothers, the homeless, new immigrants and members of certain ethnic minority groups) [22]. It thus bears remembering that burn survivors have problems that are both complex and varied, and which must be addressed through personalized care.

3 Traumatic Experience Associated with a Burn Injury

An injury is deemed traumatic when it is life-threatening or at the least, sufficiently severe to require that the victim receive emergency care or be admitted to a hospital care unit [23]. Burn injury is a type of traumatic injury. It is common for burn survivors to report feeling extremely scared or powerless at the time of the events, when they did not know whether they would be disfigured, disabled, or even survive. Feeling as though one's life is threatened increases the risk of a person experiencing psychological complications [24, 25].

The arrival of rescuers on the scene does not necessarily equate the end of the traumatic experience. Several patients have spoken of being highly stressed at the time of their admission to the care unit. A stay in the intensive care unit (ICU) can also contribute to the traumatic experience. Persons receiving critical care are three times more likely to develop PTSD than those for whom this type of care is unnecessary [26]. Treating major burns can be very difficult, even traumatic, specifically due to the intense pain and repeated surgical procedures [27], which can even include amputation of a limb. Also, finding oneself in delirium, especially when accompanied by psychotic symptoms such as intense paranoia or scary hallucinations, can prove to be a traumatic experience [28].

4 Early Psychological Reactions

Intense emotional reactions are often observed in the hours and days following a burn injury [29]. A study on this topic revealed that during the first

2 weeks after being burned, 76% of participants claimed to have difficulty falling or staying asleep, 59% stated that they relived the event, 40% felt intense distress when reminded of the event, 29% had nightmares or bad dreams, 50% claimed to avoid any feelings or thoughts of the event, and 27% refused to speak of the event [30]. Half of the persons involved also experienced some type of dissociation (distorted perception of time, blackouts, or memory gaps).

In addition to post-traumatic reactions, major burn survivors are likely to present a wide variety of emotional reactions such as sadness, anger, guilt, and fear [29]. Depressive reactions are very common in people who have suffered severe burns. This emotion can be linked to various losses: a home that has burned to the ground, the inability to continuing doing one's job, the amputation of a limb, disfigurement, the death of a loved one, etc. Experiencing pain, particularly when it is constant or in the background and linked to therapeutic actions, has a significant impact on a patient's mental state. Other factors that can impact a burn survivor's morale include a limited social or support network, being far from home or family, and work-related problems.

5 Mental Health Disorders

While most of the studies conducted addressed the psychological after-effects of severe burns on patients, around one-third of survivors present with a premorbid mental disorder, and more specifically depression or substance abuse [31, 32]. Other issues include psychosis, personality disorders, and neurocognitive disorders [14, 33, 34]. The *de novo* psychiatric disorders observed most frequently after major burns are delirium, post-traumatic stress disorder (PTSD), and major depressive disorder (MDD) [35]. Their usual occurrence and associated symptoms are depicted in Fig. 1. Other mental health problems can surface during the year after the event, among them general anxiety disorder, social anxiety disorder, alcohol or drug use disorders, sleep disorders, body dysmorphic disorder, and sexual dysfunctions.

One of the major challenges faced by health care teams involves identifying those hospitalized patients with the greatest risk of developing a mental health disorder in the first year after suffering major burns. These patients should be the first to benefit from specialized early interventions.

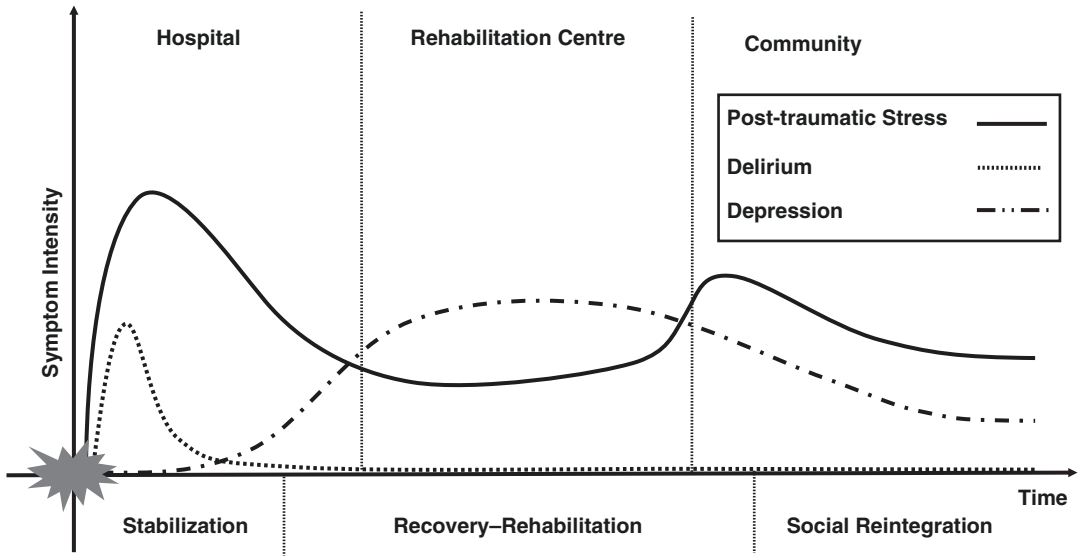

Fig. 1 Evolution of Psychiatric Symptoms after Burn Injury. (Adapted from Bergeron [36])

Table 1 Clinical characteristics of acute mental health presentations following a burn

Characteristic	Delirium	Acute stress disorder	Depression
Initial presentation	Reduced awareness of environment	Fear	Dysphoria
Onset	Acute	Acute	Discreet
Evolution	Fluctuating	Persistent	Persistent
Vigilance	Disturbed	Enhanced	Normal
Attention	Disturbed	Diminished	Diminished
Orientation	Disturbed	Normal	Normal
Memory	Disturbed, weak encoding	Traumatic memories sharp and overwhelming or fragmented	Unequal, inconsistent
Speech	Incoherent	Coherent with fears and apprehensions	Coherent with ruminations
Affect	Labile	Terrorized, anxious	Sad, diurnal variation
Psychomotor activity	Increased or diminished	Increased, especially with stimuli evoking trauma Slower with dissociation	Slower
Perception	Frequent hallucinations, illusions, or paranoia, generally unconnected to trauma	Flashback, occasional hallucinations or illusions, generally connected to trauma	Usually normal, occasional hallucinations or delusions, generally mood-congruent
Sleep	Sleep-wake cycle reversal	Nightmares, insomnia	Insomnia or hypersomnia

Adapted from Bergeron [48]

5.1 Delirium

Delirium, as a manifestation of cerebral suffering, is an acute confusional state that develops over a short period of time and shifts in intensity over a period of 5–15 days or longer. A delirious patient is less aware of his environment and may also experience disorientation as to time, place, and person. Their ability to think, pay attention, and create memories is disturbed, and he may present with hallucinations, delusions (usually paranoid), and agitation. There are three subtypes of delirium, classified by psychomotor activity: hyperactive, hypoactive, and mixed.

A person with hyperactive delirium is agitated, sometimes aggressive and has a high degree of emotional lability. This type of patient will not cooperate with medical caregivers, to the point of striking them, and can display behavior such as pulling out various tubes or IVs. A traumatized victim exhibiting hypervigilance and flashbacks could be mistakenly diagnosed as suffering from delirium. Hypoactive delirium, as its name indicates, is generally associated with an overall drop in activity or unusual apathy. It is often mistakenly diagnosed as depression. Lastly, there is the mixed subtype, which comprises an amalgam of the previous two subtypes of delirium. Table 1 compares the respective characteristics of delirium, acute stress disorder, and depression to allow for more easily distinguishing them.

Delirium is often observed in persons hospitalized for severe burns, as the result of major medical comorbidities (inflammation, infection, shock, hypoxemia, etc.) and the large doses of analgesics (especially opiates) administered. Moreover, substance abuse (alcohol, tobacco, drugs) or neurocognitive problems—two issues associated with delirium—are often observed among this group.

The reported prevalence rates vary between 15% and 77% [35, 37–39], with the highest rates found among ventilated burn survivors [40]. It is estimated that around 20% of major burn survivors will become delirious while hospitalized. This phenomenon is usually linked to a poor prognosis, namely a higher mortality and an extended hospital stay. While delirium is usually a reversible acute illness, the elderly often exhibits a worsening of premorbid dementia or persistent cognitive problems [41, 42]. Some high-voltage electric burn survivors also mention having persistent cognitive problems [43].

A person who suffers from delirium is generally not able to differentiate between perceptions (paranoia) and reality, which may lead to feeling threatened, powerless, and terrified. Memories of fear or psychosis (associated with delirium) increase the risk of developing a post-traumatic stress disorder [44]. While it is infrequent, burn survivors can develop PTSD associated with delirium experience.

5.2 Post-traumatic Stress Disorder

As described earlier, post-traumatic reactions are frequent and expected, but more severe responses may occur. It is estimated that around 15% of major burn survivors will develop an acute stress disorder (ASD), i.e., a psychiatric disorder having occurred in the first 4 weeks after a traumatic event. A diagnosis of post-traumatic stress disorder (PTSD) will rest on similar symptoms but cover a period of more than 1 month. PTSD is slightly more prevalent (20%) than ASD among burn survivors, partially explained by delayed presentation.

In fact, studies report between 2% and 30% of burn survivors will suffer from an acute stress disorder (ASD) and between 9% and 45% meet the criteria for PTSD during the year following the traumatic event [45]. This percentage varies from one study to another, depending on the tools used and the size of the sample. Both disorders are diagnosed if post-traumatic symptoms cause significant distress or interfere in patient's capacities to participate in his recovery. These symptoms are in five categories: arousal, intrusion, avoidance, negative mood and cognition, and dissociation.

Arousal manifests itself as high alertness, hypervigilance, irritability, and insomnia. The burn survivor remains on guard against (often undefined) threats and may also be startled by unexpected noises. Intrusive distressing memories may occur spontaneously as nightmares or flashbacks but also may be triggered by anything that is reminiscent of fire such as a red light or hot drink. Many patients claim to be very upset when they relive the event, which leads them to avoid doing so. An avoidance reaction should be suspected if the victim apologizes repetitively for not being able to share the story of the event that has caused the burn injury. Persistent negative emotional states (fear, anger, or guilt) and beliefs about oneself or the world interfere with recovery and capacity to receive empathetic support from loved ones. Finally, dissociative symptoms present usually early after the trauma as being in a daze or memory gaps.

5.3 Major Depressive Disorder

Between 4% and 10% of major burn survivors will present with a major depression in the year following their injury [46]. A significant percentage (22–54%) of burn survivors will exhibit symptoms of depression, even if they fail to meet all of the diagnostic criteria for depression. Suicidal ideations may develop in burn survivors and it is associated with pain severity experienced at hospital discharge [47]. In addition, rates of self-harm have been shown to increase significantly following a burn injury [20]. It is important that the burn survivor be screened for depression and that treatment should be offered accordingly.

5.4 Risk Factors Associated with Psychopathology After a Burn Injury

The primary risk factors observed among major burn survivors and drawn from two literature reviews [49, 50] and one meta-analysis [45] are listed in Fig. 2. Studies focus mostly on PTSD symptoms but also on depression and anxiety. The factors considered as being the most likely to predict a burn survivor's psychological evolution do not include burn severity indicators (such as total body surface area burned and duration of the hospital stay) [45, 50]. These findings underscore personal characteristics such as gender and personality, the pain experienced and factors that play a role in one's ability to adapt to the event (e.g., mental problems, social support, adjustment styles).

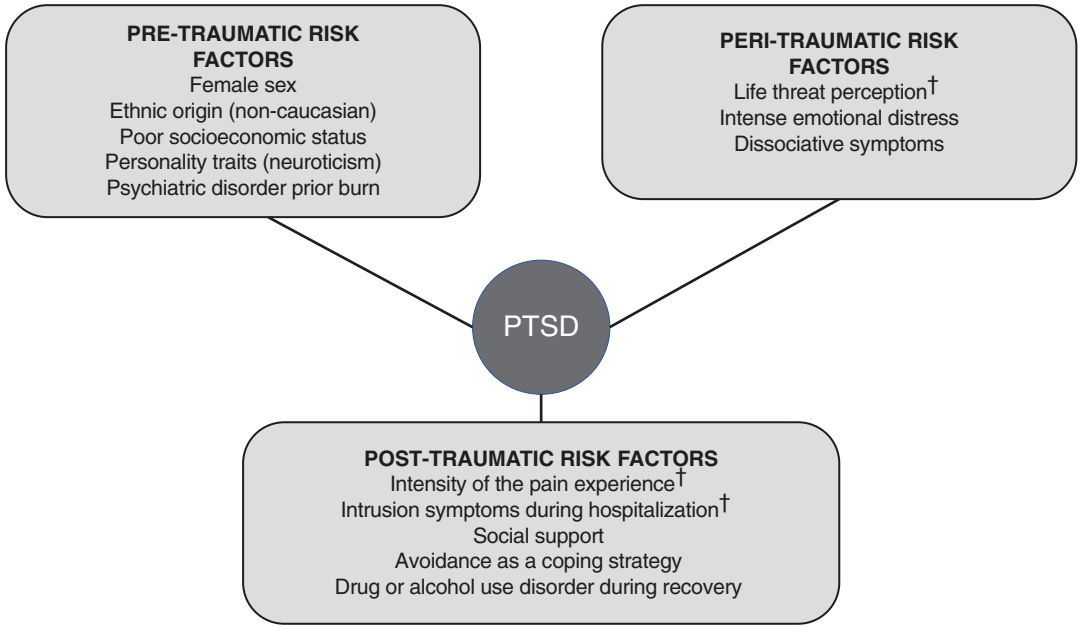

Fig. 2 Factors associated with an increased risk to develop PTSD in burn survivors. (Adapted from Bond and Bergeron [52])

Although few protective factors have been identified thus far, a more beneficial element was observed in patients with a stable social network [7]. Conversely, a "negative" social support system appears to be closely linked to more severe post-traumatic symptoms [51]. Problems getting used to changes in one's appearance and burn scars has recently been identified as another predictor of PTSD [24].

Summary Box: Sects. 1–5

While the experience of burn injury is associated with intense psychological reactions that will usually vanish over time, burn survivors have a higher rate of premorbid mental health problems, and a higher lifetime risk of mental health disorders. The most common *de novo* mental health conditions seen after burn injury are delirium, post-traumatic stress disorder, and major depressive disorder. Mental health conditions in burn survivors can be associated with worse medical outcomes, longer hospital length of stay, and poorer quality of life. As a result, it is imperative that the mental health needs of the burn survivor are addressed to optimize the recovery process.

6 Mental Health Care on a Burn Unit

Mental health evaluation and monitoring of burn survivors should be systematic, proactive, and focused on prevention, particularly given that the approach that favors waiting has been proven ineffective [7, 27, 53]. The initial assessment need not be carried out by a mental health expert and can be initiated by any member of the care team.

The term "psychological care" was proposed to describe the set of psychological interventions designed to support burn survivors during their recovery [49]. This term seeks to standardize psychological interventions and in so doing, intimates that they could be beneficial for all burn survivors. Despite numerous attempts to describe the psychological care that should be extended to

major burn survivors [7, 8, 10, 27, 29, 53, 54], a unique intervention model has yet to be created.

Based on the scientific literature and our professional experience, the following interventions are recommended and conducted depending on a burn survivor's needs:

- Develop a relationship built on trust
- Appreciate patient history and risk factors
- Evaluate and normalize early psychological reactions
- Provide psychological first aid tailored to the hospital setting
- Foster social support
- Support the management of pain, anxiety, insomnia, and delirium
- Administer adjunctive pharmacological treatment

Nurses and rehabilitation team members, given their close proximity to these patients, are often the best persons to deliver general psychological care such as empathic listening and reassurance, meeting basic needs, providing information on initial psychological reactions and labeling them as normal, teaching pain and anxiety management techniques, coaching loved ones on how to provide social support and overseeing the completion of screening questionnaires.

6.1 Hospital-Based Psychological First Aid

The belief that victims should be encouraged to talk about their experience as soon as possible after a traumatic event is still alive and well in the general population as well as among medical personnel. However, numerous studies have revealed that not only do debriefing interventions fail to reduce the risk of developing PTSD among participants, but they can also increase it, compared with the control group [55, 56].

Psychological First Aid (PFA) has been developed as an alternative approach that combines a series of strategies designed to improve the coping ability of trauma victims while promoting resilience [57]. When caring for burn survivors, all health care professionals can employ those strategies outlined in Table 2.

Table 2 Hospital-based psychological first aid for burn survivors

Contact and engagement	• Introduce yourself (name, title, and role) • Focus on the present and reassure the victim • Ask whether there is anything you can do to help • Suggest having a short conversation • Explain the upcoming steps
Safety and comfort	• Ensure that the patient is physically comfortable • Alleviate pain • Protect the patient from additional stressors
Stabilization	• Calm the patient when he is in distress or seemingly on guard • Orient if confused • Listen to the spontaneous recounting of events, losses, worries, difficulties, and emotions, all without ever pushing a patient to provide specific details about these occurrences or feelings
Information gathering on current needs and concerns	• Ask questions regarding a patient's immediate needs and worries • Identify any related questions or concerns • Flag any discrepancies between the concerns of the burn survivor and those of his loved ones • Ask questions about cultural differences based on the burn survivor's ethnic origin or beliefs, to allow for making any necessary adjustments to the care provided
Practical assistance	• Offer practical help with immediate short-term needs (e.g., getting the patient a glass of water, contacting his loved ones) • Ensure that the details regarding the burns, the care received and other needs have been obtained, or followed up

(continued)

Table 2 (continued)

Information on coping	• Validate the patient's emotional reactions • Discuss the reactions to stress, and specifically how they are normal and expected • Reassure the patient that everyone recovers at their own pace • Advice how reactions observed will fade away, especially if they are accepted rather than avoided • Respect the coping strategy chosen by the burn survivor, including denial during the first few weeks after the burn • Promote self-control by encouraging the patient to rally and to start performing small tasks • Promote a regular routine and scheduled (hence predictable) health care • Identify the triggers that remind the patient of the traumatic event and teach emotional self-control skills • Identify avoidance behaviors and if appropriate, teach the principles of exposure
Connection with social supports	• Encourage and facilitate connections with loved ones • Provide support to loved ones and emphasize that their well-being is a key component to helping the patient
Connection with other professionals or organizations	• Reach out to physicians or other professionals to take steps with regard to a specific need • Contact professionals involved with the patient prior to the traumatic event • If necessary, refer the patient to specialized mental health services in his region • Cooperate with community workers and organizations involved in the patient's psychosocial support and social reintegration

Adapted from Bond and Bergeron [58]

6.2 Supporting the Supporters

One of the key aspects of caring for burn survivors is the support of spouses and loved ones [8]. Caregivers must ensure that loved ones are not neglecting their own fundamental needs [59], such as eating or sleeping. This is particularly critical when we consider that adequate social support is known to be one of the most important factors in post-burn recovery [60–62] and appears to protect survivors from PTSD [63].

Loved ones, however, can find it hard to take on a caregiver role, likely because they are still recovering from the shock of what occurred [64]. In some cases, the loved one was even present at the time of the event and thus also intimately affected by the traumatic experience. Reactions from loved ones are similar to those of burn survivors: numbness, anxiety, panic, reliving of the event, difficulty concentrating and sleeping, constant state of vigilance, and a tendency to avoid everything associated with the event [59, 64, 65]. Therefore, a critical component in caring for burn survivors is helping their support network.

Loved ones need information to understand what is happening to the burn survivor as well as advice on the best way to help [8, 27]. Some suggest that explaining the recovery steps in cases of major injuries can help loved ones better understand the sequence of future events and foster feelings of hope as well as a greater sense of control [59, 66]. Psychological manifestations experienced by burn survivors, such as delirium, post-traumatic reactions, and feelings of pain, should also be reviewed with loved ones so that they can best help support the recovery of the burn survivor [10].

6.3 Delirium Management

To date, there has been no research on treating delirium among burn survivors. The global management of delirium summarized in Fig. 3 rely on restoring organ function, treating medical conditions (such as infection) and ceasing or reducing medication (such as opiates or benzodiazepines) that may cause delirium. Agitation and psychotic symptoms often call for psychopharmacological treatment but behavioral and environmental interventions should always be part of delirium care.

Non-pharmacological interventions are often grouped in a multicomponent bundle of care and include adequate oxygen delivery, pain relief, hydration, nutritional assistance, sleep management, revision of polypharmacy, regulation of bladder and bowel function, early mobilization, and correction of visual or hearing impairment. This approach has shown a significant reduction in delirium incidence [67–70] and the use of a sys-

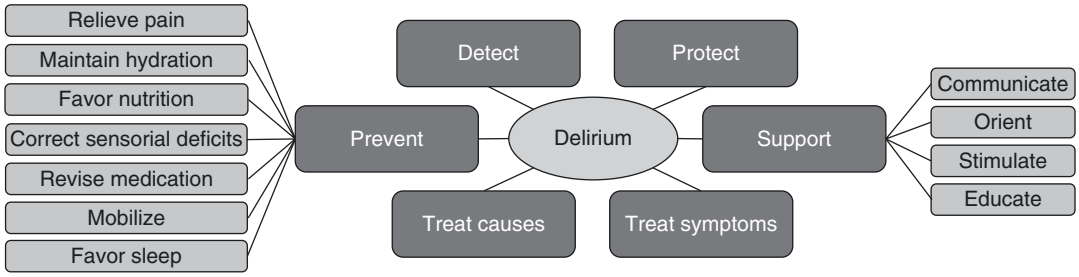

Fig. 3 Comprehensive approaches to managing delirium. (Adapted from Bergeron [73])

tematic multicomponent intervention strategies for the prevention of delirium is recommended.

Systematic detection of delirium with the use of monitoring tools like the Intensive Care Delirium Screening Checklist (ICDSC) [71], the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) [72] enhanced the skills of the medical team to assess this confusional state even with patients mechanically ventilated.

Current evidence does not support the use of antipsychotics for prevention or treatment of delirium, and there are very few clinical studies based on a solid methodology to warrant its use on a regular basis [74–78]. However, if the patient requires rapid management of agitation or experience florid psychosis, haloperidol is widely accepted as a symptomatic treatment.

With a safe QTc interval and constant cardiac monitoring, intravenous haloperidol is the route of choice with regular dosage of 0.5–1 mg every 8–12 h for mild agitation, 2–2.5 mg every 6–8 h for moderate level and 2.5–5 mg (or even 10 mg) to 4–6 h for severe agitation. Haloperidol is usually started with the same dosage range and administrated every 30–60 min to obtain calm. Elderly or frail patients may require only half of those dosages. With appropriate monitoring, intravenous haloperidol may be tolerated for values of QTc superior to 450 ms, but its use is not recommended over 500 ms. When intravenous access is not available or when clinicians prefer to engage the patient in his treatment, enteral haloperidol may be offered before intramuscular, subcutaneous, or intravenous route.

Second-generation antipsychotic drugs such as quetiapine could also help alleviate symptoms of delirium and are less likely to have extrapyramidal adverse effects than haloperidol [76] which may occur more often with younger patients. They may also have less effect on QTc prolongation and risk of life-threatening tachyarrhythmia. The sedative effect of quetiapine can help to facilitate the control of agitation and promote sleep. Low dose of 12.5–25 mg once or twice a day may be sufficient for frail or elderly patients but stronger dose such as 100 mg up to three times a day may be necessary for more severe agitation. Further research is needed on the efficacy of routine use of antipsychotics in the treatment of specific symptoms of delirium like agitation.

Dexmedetomidine is an alpha 2 agonist sedative agent used in context of critical care that is preferred to benzodiazepines such as midazolam or lorazepam to reduce length of delirium and control agitation [74]. In the cases of delirium associated with alcohol or benzodiazepines withdrawal, lorazepam (0.5–2 mg) or diazepam (2.5–10 mg) is usually utilized with intravenous or enteral route [79]. Using equivalence tables, benzodiazepines are administered according to different approaches with loading dose regimens, fixed dose regimens, or according to withdrawal symptoms and then gradually reduce. Medical teams may be helped by the use of a protocol with the revised Clinical Institute Withdrawal Assessment for Alcohol (*CIWA-Ar*) Scale, but often the contribution of alcohol or sedatives withdrawal is not so clear in the confused burn patient with unknown history of substance abuse. Initial management of agitated patients may require a mix of a benzodiazepine and an antipsychotic. Along with supportive care, thiamine supplementation is also recommended in delirious alcoholic patients.

6.4 Early Psychopharmacotherapy

For patients with a prior history of mental health disorders (such as schizophrenia or major depressive disorder), a consultant psychiatrist will

quickly ascertain whether the existing pharmacological treatment should be maintained or changed in order to prevent the re-emergence of the premorbid psychiatric disorder. In order to alleviate debilitating symptoms such as insomnia, overwhelming anxiety, repeated panic attacks or agitation, a physician could resort to administering a limited amount of a psychotropic agent for a short period of time. Before this type of medication can be prescribed, a comprehensive medical evaluation must be conducted to identify any intolerances or potentially adverse effects.

Treatment of pain and comorbid anxiety is paramount after burn injury. While opiates are considered cornerstone of pharmacologic pain management of hospitalized burn patients [80], the use of adjunct agents is often mandatory [81, 82] and are described in Chap. 8. Patients with high levels of pain and high anticipatory procedural anxiety may benefit from anxiolytic therapy [83].

Benzodiazepines such as midazolam, lorazepam, oxazepam, and clonazepam are frequently prescribed fast-acting antianxiety agents that have proven effective. Like opiates, they can have a depressant effect on a patient's mental state and they should be administered prudently. If taken over lengthy periods, they can cause cognitive problems and addiction. Furthermore, their use is associated with causing or worsening symptoms of delirium and should be avoided or used with caution in critically ill patients or the elderly.

Administering high doses of morphine appears to deter the development of post-traumatic symptoms in children who have been severely burned [84], with the mechanism in play not being uniquely limited to pain relief [84, 85]. On the other hand, a systematic review and meta-analysis of 18 studies involving 5236 patients revealed that benzodiazepines are ineffective for PTSD prevention and treatment, and that the risks associated with their use are greater than any potential short-term benefits [86]. Side effects of benzodiazepines include an increase in the severity of PTSD symptoms; they also promote avoidance behavior and can inhibit the actions of psychotherapeutic processes by numbing all emotions, impeding the formation of new memories (anterograde), and hindering learning. The authors suggest that this class of medication should be contraindicated for patients recently exposed to a trauma or presenting with PTSD. Once again, benzodiazepines use must thus be carefully monitored if needed.

While benzodiazepines do make it easier for patients to fall asleep, they also inhibit deep sleep, which is the most restorative phase. As such, they do not truly improve sleep quality. There are several different options to help treat acute insomnia in burn patients. They could include the use of melatonin or the short-term use of hypnotics such as zopiclone. Antidepressant drugs such as selective serotonin reuptake inhibitors (SSRIs) do not prevent the development of acute stress disorder [87–89] but trazodone or mirtazapine are utilized for their sedating effects as sleeping agents.

Lastly, and especially for patients who suffer from PTSD-induced nightmares, prazosin is an alpha-blocker with potentially interesting applications, supported by evidence-based data [90]. The related hypotension and dizziness dictate that care should be exercised with this use of this medication. The non-selective beta-blocker propranolol lauded over recent years for its impact on post-trauma memory reconsolidation [91, 92], seemingly mitigates some of the physical symptoms of anxiety but does not appear to have any type of protective effect on victims of burn injuries [93–95].

Summary Box: Sect. 6

Addressing mental health needs of burn survivors is a critical aspect of their recovery. Doing so effectively requires a stepped care biopsychosocial approach involving members of an interdisciplinary team as well as the burn survivors' family members who play a crucial role in their recovery. Management of mental health problems on a burn unit can include both psychological and pharmacological treatments. Psychological first aid is an approach that aims to provide emotional support and promote coping. Delirium management should also involve behavioral and environmental approaches, and in the cases of severe agitation can include psychotropic medications such as haloperidol.

7 Systematic Mental Health Follow-Up for Burn Survivors

A team of clinicians and researchers from Australia working with trauma survivors [23] put forth a model of psychological care that rests on personalized risk assessments for each patient while hospitalized, as well as regular re-evaluations (watchful waiting) after their release, in the case of those who exhibit a significant risk of developing a mental problem of some sort (see Fig. 4). The authors suggest a 4-week waiting period after the patient's release before screening, as this will allow any temporary reactions to dissipate. This model is also recommended for burn survivors [96].

7.1 Step 1: Assess the Risk of Psychological Complications

This step, conducted while the patient is hospitalized, is based on the Post-traumatic Adjustment Scale (PAS) [25]. Verified among individuals hospitalized following a serious injury, this is the first self-administered scale that makes it possible to identify persons at risk of developing PTSD or becoming depressed subsequent to a traumatic event. The PAS is not a screening tool, being more focused on prediction. This tool facilitates the quick and systematic evaluation of all patients hospitalized following an injury at a low cost.

7.2 Step 2: Set Up Watchful Waiting and a Screening Process

This step is put into place once the patient has been released from the hospital. It solely concerns those people who present a significant risk of developing psychological issues associated with their burns. While the monitoring/follow-up model may initially appear simple, its implementation calls for significant efforts in terms of logistics and acceptability. Mental health monitoring is generally combined with medical follow-up. Table 3 provides a few suggestions [97, 98] regarding screening tools that burn survivors can turn to.

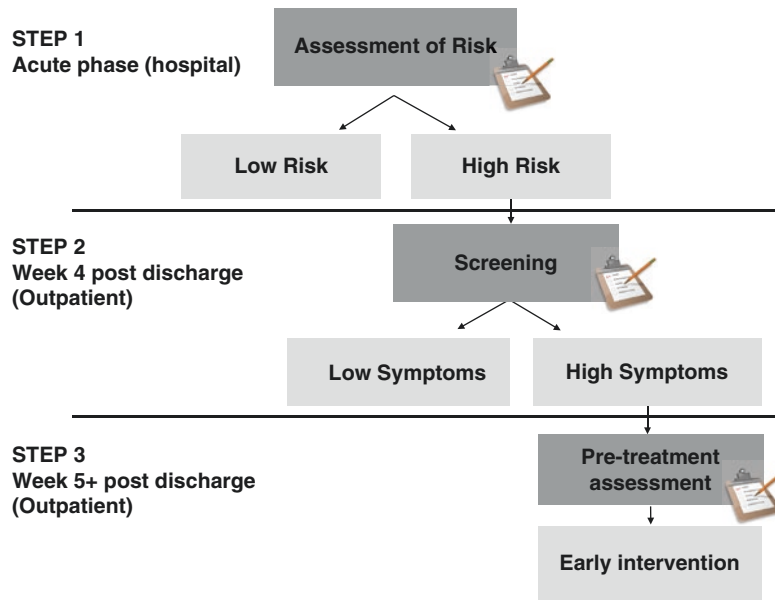

Fig. 4 Model of systematic follow-up for burn survivors (Adapted from O'Donnell et al. [23])

Table 3 Recommended measures to screen for psychological issues related to burns

Element evaluated	Suggested measures
Difficulties specifically associated with the burns	Burn Specific Health Scale-Brief (BSHS-B)[1, 3]
Post-traumatic reactions	PTSD Checklist for DSM-5 (PCL-5)[1, 2, 3]
Depression	Patient Health Questionnaire (PHQ-2, PHQ-9)[1, 2, 3]
Anxiety	Generalized Anxiety Disorder (GAD-7)[3]
Anxiety and depression	Hospital Anxiety and Depression Scale (HADS)[1,3]
Pain	Brief Pain Inventory (BPI, BPI-SF)[2,3]
Sleep disorders	Insomnia Severity Index (ISI)[2,3]

Notes. [1]Measure recommended by the American Burn Association Gibran et al. [97]
[2]Measure recommended by Mason et al. [98]
[3]Measure recommended by the authors of this chapter
Adapted from Bond and Bergeron [99]

Table 4 Key elements of cognitive behavioral therapy (CBT) for burn survivors

Therapeutic	Target
Psychoeducation	PTSD, depression
Relaxation and breathing	PTSD (anxiety and hyperalertness)
Pain management	Pain, depression
Behavioral activation	Depression, social reintegration
Sleep hygiene	PTSD, sleep disorders
Exposure through imagination (memories of the event)	PTSD
Exposition *in vivo*	PTSD, depression, scars, social reintegration
Cognitive restructuring	Inadequate thoughts with regard to one's self (skills, physical attraction), others and the world
Practicing expected social interactions	Appearance and scars, social reintegration

Adapted from Cukor et al. [104], Table 1, p. 186

7.3 Step 3: Provide Early Specialized Treatment to Those Who Need Care

While numerous patients might be helped by low-intensity interventions, such measures may not be adequate for those who suffer from PTSD or a more serious depression. The best practices in terms of care for burn survivors recommend that all persons with a psychiatric or psychological disorder be referred to a specialized mental health care provider [97].

Despite the many challenges encountered during psychological recovery following major burns, research in this field is still at an early stage. To date, there have been no random and controlled studies designed to assess the effectiveness of individual psychotherapy that takes into account the main problems likely to affect burn survivors. In the presence of PTSD, trauma-focused cognitive behavior therapy (TF-CBT) or EMDR (Eye Movement Desensitization and Reprocessing) is recommended [100, 101].

While PTSD is one of the problems that most often develop following major burns [12], various other troubles can also occur, either alone or in comorbidity. The interventions adopted for burn survivors must be tailored to this clientele and address issues such as scarring, body image, chronic pain, and sexuality. This is particularly difficult when we consider that PTSD and difficulties relating to one's image can mutually reinforce one another [102]; this also applies in the case of chronic pain [45]. Table 4 illustrates some of the techniques from CBT that can be utilized in the treatment of patients with complex burns [103].

Psychotherapy focused on trauma, it must be outlined, is more effective than pharmacologic treatments in PTSD [105]. However, for patients who are more severely affected, pharmacotherapy can bring about a reduction in the intensity of PTSD and depression symptoms and facilitate patient commitment to rehabilitation or psychotherapy. The attending physician or psychiatrist selects a pharmacological agent based on patient needs and preferences and while taking into account guidelines and evidence-based practice developed by experts. Table 5 highlights medications that have first-line evidence in the treatment of MDD [106]

Table 5 Canadian Guidelines for first-line treatment in major depressive disorder (MDD) and post-traumatic stress disorder (PTSD)

First-line evidence	Medication	Daily dosing range
	Selective Serotonin Reuptake Inhibitors (SSRIs)	
MDD, PTSD	Sertraline	50–200 mg
MDD	Citalopram	20–40 mg
MDD	Escitalopram	10–20 mg
MDD, PTSD	Fluoxetine	20–60 mg
MDD, PTSD	Paroxetine	20–50 mg
MDD	Fluvoxamine	100–300 mg
	Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)	
MDD, PTSD	Venlafaxine XR	75–225 mg
MDD	Desvenlafaxine	50 mg
MDD	Duloxetine	30–60 mg
	Other Antidepressants	
MDD	Bupropion XL	150–300 mg
MDD	Mirtazapine	15–45 mg
MDD	Vortioxetine	19–20 mg

Adapted from Kennedy et al. [106] and Katzman et al. [100]

and PTSD [100]. Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs) deserve special attention given their evidence and safety in treatment of comorbid neuropathic pain in burn survivors [107].

Summary Box: Sect. 7

All burn survivors should be evaluated during acute care for their risk to develop later psychological complications and then reassessed 4 weeks after their discharge from the hospital. For those who have developed mental health problems such as PTSD or depressive disorder, they should be referred to specialized mental health services to obtain evidence-based treatments such as cognitive behavioral psychotherapy, and if necessary psychopharmacotherapy.

8 Post-traumatic Growth

While the majority of this chapter has focused on the mental health challenges faced by burn survivors, it is also important to reflect on the concept of post-traumatic growth (PTG), which has been a recent area of study in this population. The concept of PTG is that positive psychological changes can happen as the result of a traumatic event in domains such as appreciation of life, relationship with others, discovering new possibilities in life, increasing personal strength, and spiritual change [108].

This concept of PTG has been recently studied among burn patients. In a longitudinal study done in Australia, they showed that depression is strongly linked to a lack of PTG, indicating the importance of addressing these symptoms early on in a patient's path towards recovery [109]. Furthermore, it has been shown that the sudden nature of the burn injury and severity and location of the injury can impact PTG. In addition, an integrative literature review of PTG in burn patients illustrated common themes that can support PTG. A model [108] is proposed in Fig. 5.

Chapter Summary

Burn injuries are a devastating experience for victims and their loved ones. They notably have significant impacts on a burn survivor's physical and mental condition. A significant number of survivors will experience difficulties adapting and ultimately, develop one or more disabling psychiatric disorders. The severity of the injuries and psychological issues are the factors with the most significant repercussions on the quality of life of burn survivors. It is imperative that a systematic biopsychosocial approach be taken to help support the mental health challenges faced by burn survivors in their path towards rehabilitation from admission on the burn unit to their social reintegration. Mental health care constitutes a major challenge for caregiver teams throughout the recovery process and its integration must be upheld by a moving and persistent conversation in this regard.

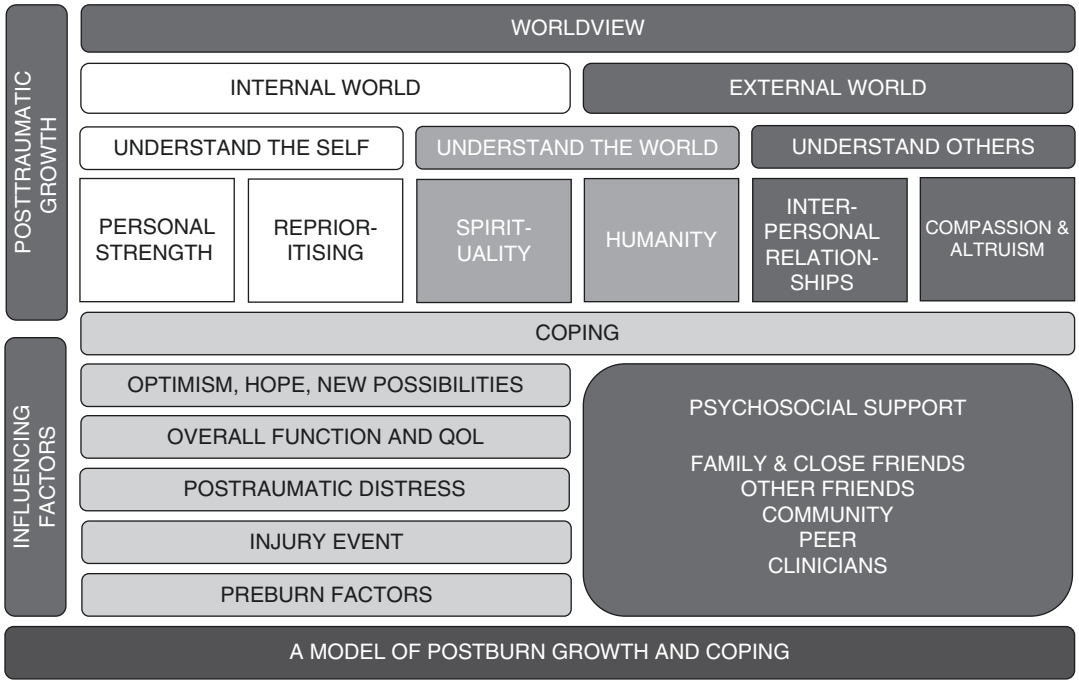

Fig. 5 A model of post-traumatic growth in burn patients. (Adapted from Martin et al. [110])

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Burn Outcomes

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What gets measured gets managed

—Peter Drucker

1 Introduction

The following chapter describes important outcomes in the recovery trajectory of burn survivors. Thanks to improvements in critical care, many burns that were fatal 50 years ago are survivable today. Due to this increased survivability burn survivors are faced with a greater sometimes lifelong, symptom burden. As a result, attention has been placed on improving care for persistent conditions with the goal of improving quality of life. To this end, consistent and accurate measures of outcomes that matter to burn survivors and can inform treatment options are essential to drive and assess improvements in care. Outcomes of interest can be broadly categorized into those that deal with scar, function, and mental health including quality of life.

No previously published material requiring permissions was used in the chapter Burn Outcomes.

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2 Outcomes

It is important to understand outcomes in the context of the biopsychosocial model of injury [1, 2]. The model incorporates various injury-related factors in the context of three distinct time periods (Table 1). Research demonstrates that pre-injury factors are determinants of injury occurrence and sequelae following injury [3–7]. Factors related to the clinical care of the patient are part of the growing field of quality improvement [8]. The current review will focus on post-discharge factors including the patient's return to their pre-injury environment and activity. As these factors are consequences of both injury and care, they will be referred to as "Outcomes."

Outcomes are of two types: those which can be measured objectively, and those which are reported subjectively. Objective outcomes include: scar assessments, mental and physical

Table 1 Factors by time period

Pre-injury: determinants	Inpatient stay period: performance indicators	Discharge and life course: outcomes
Demographics	Injury cause	Function
Physical conditions	Treatment	Scar
Psychological conditions	Length of stay	Quality of life
	→ Time	

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disorder diagnoses, and return to function or work. Subjective outcomes are also of great importance and include: pain, pruritis, paresthesia, body image satisfaction, and perceived health and function. Some outcomes are reported as a composite of subjective and objective measures. Although objective measurements yield quantitative results that are easier to compare, it is still difficult to evaluate the interactions between factors, and the outcome's impact on the patient's quality of life. For example, a scar may have only mild erythema, but be very pruritic causing a significant quality of life impact.

Accurate measurement of outcomes require instruments that are reliable, valid, and responsive. These terms mean, respectively, that the instrument returns consistent values upon repeated measurements, that it measures what it purports to measure, and that it can detect change within the range of interest. This chapter focuses on tools that are valid and have their reliability reported. Outcomes of interest have been grouped in the context of the patient journey, starting with the scar, the effect of scar on function, and the overall effect of the injury on the burn survivor's health.

3 Scar

Subjective and objective scar measurement instruments are known as scales and tools, respectively. Scar scales are efficient and easy to implement and do not require an experienced therapist. In contrast, scar tools which provide objective measurement of scar qualities are expensive and require time and training, an exception being digital photography. For assessing treatment methods, both scales and tools are useful. However, because of training, cost, and time commitments many tools are not in widespread clinical use.

Some scales include subjective qualities like pain and itching which patients rate as more important to them than appearance [9]. Those qualities can also compound the psychological impact of the scar. A patient's overall assessment of their scars has been shown to correlate with depression [10]; however, scar scales do not usually include this psychological measures. A quality of life scale can be a useful addition for measuring the global impact of the scar.

The measurable qualities of scar can be categorized as below [11, 12]:

- Color: vascularization and pigmentation
- Dimension: elements of size and thickness
- Texture: irregularity, and matte or shininess
- Biomechanical Properties: pliability, elasticity, and water retention
- Mobility Restriction: freedom of movement of the affected limb or area

Two widely used scar scales are the Vancouver Scar Scale (VSS) [13] and the Patient and Observer Scar Assessment Scale (POSAS) [14]. There are several other scales in use including the Hamilton and Manchester Scar Scales, MAPS, and the Inventory of Potential Reconstructive Needs scale [11]. However, there is no consensus on a best scale.

In the Vancouver Scar Scale, the caregiver rates pigmentation in three levels, vascularization and thickness in four levels each, and pliability in six levels. The scar is given a total score from 0 to 13. Modifications to the VSS exist which include itching and pain categories. These categories are patient rated on a visual analog scale, often a 100 mm line marked at the end points by "none" and "extreme." Another modification to the VSS exists which allows for a more accurate pigmentation rating for non-Caucasian patients [15].

In the POSAS, all categories are rated from 1 to 10. The patient rates pliability, thickness, color, relief, pain, and itching while the observer rates pliability, thickness, vascularization, pigmentation, surface roughness, and surface area. All scores are combined to give a total score.

A scale's reliability is its tendency to produce similar values upon repeated application, either when applied repeatedly by the same observer (intra-observer reliability) or by different observers (inter-observer reliability). A frequently used measure of the latter is Intra-class Correlation Coefficient (ICC), which is a value between 0 and 1 representing reliability. ICC values above

0.75 are considered "good" and those above 0.9 "excellent." [16] In a study on linear surgical scars, POSAS had an ICC of 0.86 [17]. The VSS, in a burn population, had an ICC of 0.81 [18]. Early scar scales had poor reliability [11]. To remedy this, multiple observers would rate the scar and average their scores, thus reducing variance. POSAS itself is a sum of patient and observer scores, and this is a possible reason why its reliability is higher than the VSS.

Several scar measurement tools report higher reliability than what can be achieved with scar scales. However, not all tools have been studied in detail and their reliability is yet to be determined. Some reliable tools include 3D cameras which can measure scar surface area to within 2% [12]. The DSM II Colormeter measures erythema and pigmentation based on how melanin and hemoglobin absorb red and green light. Its ICC for the measurement of melanin has been reported as 0.91 and its ICC for erythema has been reported as 0.91 in one study and 0.68 in another [12]. The Cutometer, which measures skin elasticity, has a range of reported reliabilities from 0.11 to 0.93 [12]. Finally, ultrasound devices, in particular the Dermascan C was measured to have an excellent reliability of 0.9 for measuring scar thickness [12].

Digital photography, the most accessible scar rating tool, can be used to objectively measure color. Also, if electronic records can accommodate digital photographs a measure of scar progress can be transferred between caregivers.

4 Mobility, Function, and Work

Scar can affect outcomes in the domains of mobility, function, and work. These domains are loosely related yet one can have good function with poor mobility and good mobility and function but a delayed return to work. This delayed return can be due to psychological factors, skin issues, or pain. We will consider the three topics in this section.

Mobility is frequently impaired by contracture, which follow burns. Burned skin, muscle, and ligaments can tighten and scar will continue to contract for a period of time with consequences lasting years. Contractures of major joints (hip, knee, elbow, and shoulder) can impact performance of daily tasks. Treatment using splinting, casting, ROM exercises, and surgery can potentially improve mobility. Contractures frequently improve during inpatient rehabilitation. In one pilot study, 65% of major joints affected by contracture improved by at least one level of severity during inpatient rehabilitation [19] (i.e., one level corresponding to 60° mobility for the shoulder). It is interesting to contrast the success of this noninvasive rehabilitative approach with surgery, in which 88% of joints treated returned to normal function, but the remaining 12% reported adverse outcomes. It is important to measure these changes objectively in order to identify if therapy is effective, or more importantly when therapy does not improve mobility, suggesting that other options such as surgery are required.

The patients ability to perform simple tasks is predictive of their physical health-related quality of life [20]. Range of motion is commonly tracked as part of rehabilitative efforts [21]. The importance of inpatient rehabilitation has led to integrated rehabilitation services which lowers length of stay, improves resource utilization and decreases waiting times for services [22]. Early ambulation has also been found to be beneficial and early sitting while in ICU was investigated and found to be safe [23].

The simplest objective measure of joint mobility is degrees of active and passive ROM as measured with a goniometer. It is important to evaluate the progress of the patient relative to their pre-injury ROM and relative to the uninjured population. However, it must be remembered that the number of degrees may not reflect an improvement in function.

Function refers to the ability to perform simple tasks and to live independently without assistance. Information on function, which is more subjective than mobility, can be quantified using scores such as the FIM (Functional Independence Measure). The patient's ability to perform 18 simple tasks is rated from 1 (Total assistance required) to 7 (No assistance required). Assessment of function should be performed by

the clinician, not the patient. Scores above 110 indicate an ability to manage at home with no assistance. Each deficit of 5 points corresponds to 1 h of assistance needed with tasks per day. In one study, the motor component of FIM increased by 29 points between admission and discharge to a rehabilitation facility, corresponding to 6 fewer h of assistance required at home. This displays the type of progress that can be made in improving function and the utility of meaningful measures. FIM is highly reliable and has an ICC score of 0.95 [24].

The measurement of specific areas of function is still evolving in the context of burn injury. For example, hand function impairment is common in burn survivors. One instrument for its measure is the Michigan Hand Questionnaire. It has been validated for the general population although not yet the burn population. Hand function is also a domain in the nine domain model of the BSHS-B, discussed below. In a study of hand function, all patients showed improved hand function scores by discharge yet still remained below normal uninjured levels [19].

Returning to work is an important outcome in establishing a pre-injury quality of life. For a third of burn inpatients, time to return to work will be greater than 2 years [25]. Of a number of factors analyzed as predictive of returning to work, %TBSA was the most significant, followed by % Full Thickness and Length of Stay [26]. Interestingly, age was not found to be predictive. Those with a length of stay less than 10 days would return to work within on average 2 months, while those with a length of stay greater than 30 days took longer than 2 years on average to return to work [26]. Further predictors of a greater than 1 year return to work were: the occurrence of a burn at work, an etiology of electrical burn, and receiving inpatient rehabilitation [25].

Barriers to returning to work, as reported by burn survivors were, in order: pain, neurologic problems, impaired mobility, and psychiatric problems [25]. As both physical and psychological problems must be overcome, returning to work demonstrates excellent adaptation to the injury including good progress in the domains of function and mobility, and is therefore a useful indicator of recovery progress.

5 Development of Post-discharge Outcomes

As burns impact physical and psychological health, it is important to consider patient-centered outcomes both in judging treatment efficacy and in establishing baselines for expected quality of life through which we can work to improve patient care.

Studies have found that distress experienced in hospital predicts chronic distress persisting through a 2-year period post-discharge [27]. High in-hospital distress occurred in a third of patients and was associated with poorer psychological health [27]. In many cases, the distress experienced by patients is subclinical yet it can have an impact rivaling physical conditions [9, 28].

In one study, the top 12 sources of distress after discharge were identified [9]. They were, in order: pain, decreased ROM, itch, temperature changes, decreased strength, disliking appearance, uncomfortable scars, skin color changes, financial concerns, long recovery time, poor sleep, and distress related to pressure garments. Patients also rated how much each source bothered them at various time points after discharge. The level of distress from those sources decreases after discharge. But temperature changes, disliking appearance, and changes in skin color took longer than a 2-year period after discharge to decrease. Distress from pain and poor sleep were found to predict a delayed return to work.

6 Quality of Life, BSHS-B, and SF-36 PROMs

PROMs or Patient Reported Outcome Measures capture outcomes that are important to the patient and determinable through survey responses. For conducting PROMs on a large scale, Computer Assisted Telephone Interviews (CATI) may be

ideal because of their high response rate compared to other methods [29].

A systematic review of studies using PROMs in burn survivors found the BSHS-B and the SF-36 were most widely used, each occurring in about 40% of all studies measuring life satisfaction in burn survivors [30]. The BSHS-B was designed for the burn population and is thus a disease-specific PROM. The SF-36 was designed for the general population and can therefore be used to compare impact on quality of life across condition.

The eight categories measured by the SF-36 are: physical functioning (PF), role disability due to physical problems (RP), bodily pain (BP), general health perceptions (GH), vitality (VT), social functioning (SF), role disability due to emotional problems (RE), and general mental health (MH). Results in these categories are used to score the composite areas of physical and mental health. Many investigators combine these two scores to reach a single score; however, this was not the original intent of the SF-36 designers, and this interpretation may not have validity as a quality of life measure [31].

The Burn-Specific Health Scale has undergone several improvements since its formulation [32]. Originally, a 114 item survey developed by burn care experts and patients, it was later abbreviated to 80 items as BSHS-A, revised to the 31 item BSHS-R, and expanded slightly to the 40 item BSHS-B [33]. This expansion added the domains of hand function and sexuality which were missing from the BSHS-R [33]. All BSHS questions are scored on a five-point scale from 0 to 4.

The 40 items of the BSHS-B were chosen by applying a factor analysis to the items in previous scales. A factor analysis categorizes items into groups in a way that minimizes the covariance between the groups. Thus, the dependence of one category on another is minimized and each category can have a meaningful interpretation. The factor analysis resulted in nine domains. Subsequently, a second-order factor analysis was done on those nine domains revealing three meta-domains [34]. This is an alternative, psychometrically valid and simpler interpretation of BSHS-B results. The work domain was excluded from factor analysis because it was correlated with two meta-domains, Function and Skin Involvement [34].

Nine and three domain interpretations of the BSHS—B

Simple abilities	Function
Hand function	
Heat sensitivity	Skin involvement
Treatment regimens	
Body image	
Affect	Affect and relations
Interpersonal relationships	
Sexuality	
Work	

A 10-year follow-up of burn patients showed that median scores in all domains of the BSHS-B were at least 3 out of 4, indicating good recovery at the median level. [35] However, the lowest quartile of burn patients scored less than 2 out of 4 in Body Image and Heat Sensitivity, indicating those as problem areas for severe burns. Other domains showed more promising results at the 10-year mark. In another study, over the 2–7 year time frame Hand Function and Interpersonal Relations improved after discharge, but not significantly until the 2 year mark was reached [36].

7 Using Outcome Measures

It is possible to use PROMs and outcome measures in the following ways:

- Compare the effectiveness of different treatments
- Measure a patient's recovery in comparison to an expected baseline
- Compare burn center outcomes to a global average

However, challenges exist here. Firstly, it is impossible to completely standardize the burn injury. TBSA, body part involvement, and % full thickness will be different across injuries and are imperfectly estimated. Also, as noted in the Outcomes section, the patient's pre-morbidities affect their recovery [37]. Even within a burn

center, differences in treatment and rehabilitation procedures and timing can lead to different patterns of recovery. Finally, measuring long-term outcomes are challenging as patients who experience a worsening of their conditions may exit a study making the remaining population artificially healthier.

Another difficulty in measuring quality of life is untangling experienced well-being (how much happiness did you experience yesterday?) from evaluated well-being (How would you rate your life over the last year?). Experienced and evaluated well-being were only weakly correlated in 20,000 studied Americans [38]. This means that high experienced well-being is possible even when life evaluation is poor. The display of post-traumatic growth in burn survivors who retain functional impairments yet live meaningful lives is testament that a high quality of life may be possible for all survivors.

Despite the stated challenges, the evaluation and measurement of burn related outcomes is an important component of burn care. Measurement of outcomes allow us to judge treatment effectiveness accurately; know when a patient is not meeting recovery goals; and evaluate a burn center's practices to improve care. Long-term studies show that health improvement can continue to occur beyond 2 years post-injury and so there is a wide scope of interventions to make meaningful differences in the persistent conditions that affect burn survivors [36].

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Electrical Injury, Chemical Burns, and Cold Injury "Frostbite"

Shahriar Shahrokhi

1 Electrical Injuries

1.1 Introduction

Electrical injuries/burns comprise of a small portion of all burn unit admissions approximately <5%; however, they have devastating consequences and are a common cause of amputations [1–5].

These injuries are divided into high voltage (>1000 V) and low voltage (<1000 V), and the severity of the injury cause is dependent on:

- Voltage (*E*)
- Current (amperage—*I*)
- Resistance of the tissue to current flow
- Current type (AC vs. DC)
- Duration of contact

Joule's law defines the amount of tissue damage:

$$\text{Power}(J) = \text{Current}(I)^2 \times \text{Resistance}(R).$$

Electrical current can cause tissue damage through thermal and cellular injury. Thermal injury is as a result of the heat generated as the current passes through various tissue. The higher the resistance of tissue to current flow, the greater heat generated which results in greater tissue damage. The various types of electrical injury are summarized in Table 1.

The cross-sectional area of the tissue contributes to the severity of injury with greater damage seen in areas with smaller cross-sectional radius (wrists and ankles) [4, 5]. The current is hence responsible for the tissue damage not the voltage.

In addition, electrical current can cause tissue damage by altering the cell membranes properties through cellular depolarization and by forming pores in the cell membrane (electroporation); in addition, the current can lead to protein degradation by electro-conformation [6–9].

1.2 Diagnosis and Management

High-voltage injuries should be treated as with all traumas beginning with ABCDE primary survey followed by a thorough secondary survey. Up to 15% of all electrical injuries are associated

Table 1 The types of electrical injury

Electrical contact	Electrical injury caused by current flow against tissue resistance
Arc	Thermal burn caused by arcing of electrical current passing through the air from point A to point B
Flash	Thermal burn from ignition of clothing or surroundings

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with other traumatic injuries; most prevalent are the neurologic (traumatic brain injury—TBI) and orthopedic injuries (fractures) [4, 5, 10]. Many of the organ systems are affected by electrical injury, and these sequelae are summarized in Table 2.

High-voltage electrical injuries are a predominant male workforce-related injury with significant sequelae and economic cost. There are practice guidelines for the management of these injuries [20]; however, as these injuries have a low rate of occurrence, they are best managed in

Table 2 The organ system sequelae of electrical injury and proposed management

System	Sequelae	Management
Neurologic/sensory [4, 5, 11–17]	Loss of consciousness	Need to monitor patients and have close follow-up for possible delayed presentation
	Traumatic brain injury Spinal cord injury	
	Motor and sensory deficits (can be delayed) Neuropsychological problems (PTSD, depression, chronic neuropathic pain)	
	Tympanic membrane rupture	
	Delayed cataracts	
Cardiovascular [18–23]	Supraventricular arrhythmias most common, followed by ventricular arrhythmias (fibrillation most common), asystole Myocardial infarction Vascular injury (thrombosis)	Initial ECG, followed by cardiac monitoring for up to 24–48 h based on the presence of: ECG abnormalities Cardiac arrest Loss of consciousness Role of markers of cardiac damage (troponin, Ck, Ck-MB) is unknown
Respiratory [24]	Respiratory arrest secondary to paralysis of diaphragm	CPR, need for intubation and ventilation
	Pneumothorax	Treat with chest tube
Abdominal [4, 5]	Blunt abdominal injury Evisceration Ileus, gastroparesis	Treat in accordance to the priority of injury as per ATLS and trauma center guidelines
Renal [4, 5, 25, 26]	Myoglobinuria Acute tubular necrosis	Increase fluid resuscitation to maintain a urine output of 1 mL/kg/h. Some controversy regarding alkalization (with sodium bicarbonate infusion) of urine and forced diuresis (with mannitol)
Musculoskeletal [4, 5, 10, 13, 20, 27, 28]	Muscle necrosis Rhabdomyolysis	Increase fluid resuscitation to maintain a urine output of 1 mL/kg/h. Some controversy regarding alkalization (with sodium bicarbonate infusion) of urine and forced diuresis (with mannitol) Compartment decompression (fasciotomy) as necessary: Progressive neurologic dysfunction Increased compartment pressure Vascular compromise Myonecrosis Might require amputations
	Compartment syndrome	
	Fractures/dislocations	Manage orthopedic injuries with appropriate consultation
	Thermal burns	Manage as with any thermal injury to the skin The extent of the cutaneous injury does not correlate with the damage to deep tissues

Table 3 Common neurological and psychological sequelae of LVEI[a]

Neurologic	Numbness (82%)
	Paresthesia (63%)
	Pain (54%)
	Headache (45%)
	Weakness (45%)
Psychologic	Anxiety (54%)
	PTSD (54%)
	Poor concentration (54%)

[a]Adapted from Singerman et al. [29]

specialized centers adept to handling the various complications of these injuries.

In comparison, low-voltage electrical injuries (LVEI) are less common and have more varied etiologies and have less devastating initial sequelae. However, LVEI have more frequent long-term sequelae with delayed presentation and nonspecific symptoms [29–31]. The common sequelae of LVEI are summarized in Table 3. These individuals tend to have a lower rate of return to work due to these neurological and psychological sequelae [30, 31].

2 Chemical Burns

Chemical burns represent a small portion of cutaneous burns (reported from 3% to 10%); however, as with electrical injuries, they have dire consequences [32–35]. There are thousands of different chemicals in everyday use, and this section briefly discusses the general principles in the management of these injuries. These injuries have equal distribution of occurrence at home or at work (at least in the USA) [36]. In general, the severity of the chemical burn is dependent on the concentration, quantity of the agent, the duration of contact, the depth of penetration, and the mechanism of its action [32, 33]. Table 4 summarizes the different classes of chemicals and the mechanism by which they cause tissue damage.

The general principles in the treatment of chemical burns begins with safety and protecting all from exposure followed by ABCDE of primary trauma survey. The specific measures for chemical burns involve the removal of the inciting agent, treatment of systemic toxicity, specific antidotes if necessary, and local wound care [34]. The general principles for the management of chemical burns are summarized in Table 5.

Table 4 Classes of chemicals and their mechanisms of tissue injury

Class of chemical	Mechanism of tissue injury
Acid	Coagulation necrosis
Alkali	Liquefaction necrosis—deeper penetration and more severe tissue damage
Organic solutions	Dissolve lipid membranes of cells and disrupt cellular protein
Inorganic solutions	Direct binding and salt formation via exothermy

Table 5 Management principles for chemical burns

Removal of chemical agent	Removal of involved clothing
	Thorough and copious irrigation with water except for:
	Phenol—wipe off with 50% polyethylene glycol sponges [37]
	Dry lime—dust off prior to lavage [38, 39]
	Muriatic acid, sulfuric acid—neutralize with soap or lime water [38, 39]
Systemic toxicity	HF acid—hypocalcemia and ventricular fibrillation [40, 41]
	Formic acid—intravascular hemolysis, renal failure, pancreatitis [42]
	Organic solutions and hydrocarbons—liver failure [32]
	Respiratory injury—can occur with all inhaled agents and must be treated in same manner as inhalation injury [32]
Antidotes	Hydrofluoric acid—can use topical calcium gluconate if no response then consider injection of 10% calcium gluconate sub-eschar, if no response on involving a distal extremity then can proceed to either intra-arterial or intra-venous (with Bier Block) injection of calcium gluconate. Excision of the burn is the last resort if all above fails [41, 43]
	White phosphorus—lavage with 1–2% copper sulfate
Wound care	Wound dressing as for thermal burns
	Early excision of nonviable tissue
Ocular involvement	Copious irrigation with Morgan lens and ophthalmology consult [44, 45]

3 Cold Injury (Frostbite)

Frostbite is part of the spectrum of localized cold injury ranging from frostnip, chilblain to frostbite, which is associated with the greatest amount of tissue destruction. The mechanism for tissue injury in frostbite is as a result of direct and indirect cellular injury [46–49] and can be described as:

1. Cellular death secondary to cold exposure subsequent to:
   (a) Ice crystal formation
   (b) Cellular dehydration
   (c) Electrolyte disturbances
   (d) Denaturation of lipid–protein complexes
2. Progressive dermal ischemia secondary to:
   (a) Progressive microvascular insult
   (b) Microvascular thrombosis
   (c) Reperfusion injury

The clinical manifestations of frostbite are as a result of thrombotic events secondary to ischemia/reperfusion injury [46–48, 50, 51] and are classified into either superficial and deep or four degrees (first and second degree being superficial and third and fourth degree being deep):

Superficial

- *First degree*—Partial-thickness skin freezing, erythema and hyperemia, mild edema, no blisters or necrosis.
- *Second degree*—Full-thickness skin freezing, erythema, edema, superficial blisters containing clear or milky fluid.

Deep

- *Third degree*—Skin and subcutaneous tissue freezing, blue or black appearance, edema, hemorrhagic blisters with some necrosis.
- *Fourth degree*—Freezing extending through subcutaneous tissue into muscle, tendon, and bone; deep red and mottled appearance with eventual gangrene; minimal edema; extensive necrosis.

The common risk factors associated with development of frostbite include substance abuse and mental illness. The common factors are as follows [46–48, 52]:

- Mental illness
- Alcohol/drug intoxication
- Extreme of age
- Diabetic/other neuropathy
- Homelessness

In general, the management of these injuries is similar until full demarcation of the depth and extent of injury, which can take up to 4 weeks [46–48] and is summarized in Box 1. Ideally, these patients will need to be transferred to specialized centers adept at treating this unique injury. Once admitted to hospital the approach to the patient will be similar as in any trauma with primary survey using the ABCDE format. As frostbite is often associated with hypothermia, rewarming to core temperature of ≥35 °C must take place prior to treatment of frostbite [53]. Following the initial management, the Hennepin score will need to be calculated which will help quantify injury and tissue loss from frostbite [54]. As described by Nygaard and colleagues; the Hennepin score allows for a standard means to measure injury and outcomes in frostbite [54].

Imaging in the form of bone scan and magnetic resonance angiography (MRA) can guide management based on the provision of prognostic information [55–58]. The use of Technetium^{99} (^{99}Tc) triple phase bone scan when performed 48 h post injury can aid in assessing the extent of tissue damage and can allow for improved surgical outcome by accurately predicting amputation levels in approximately 84% of the cases [46–48, 52, 55, 56, 59, 60]. SPECT/CT combines the information from bone scan regarding bone perfusion and uptake with the anatomic information derived from CT, and its addition following the bone scan can improve surgical planning for deep frostbite injuries, as clear demarcation of the level of tissue loss can be ascertained with SPECT/CT well before its appearance on physical examination [61–63].

Box 1: Principles in Treatment of Frostbite

1. Admit patient to specialized unit if possible.
2. On admission, rapidly rewarm the affected areas in warm water at 37–39 °C for 15–30 min or until thawing is complete.
3. On completion of rewarming, treat the affected parts as follows:
   (a) Debride white blisters and institute topical treatment with aloe vera (antiprostaglandin) every 6 h.
   (b) Leave hemorrhagic blisters intact and institute topical aloe vera (antiprostaglandin) every 6 h.
   (c) Elevate the affected part(s) with splinting as indicated.
   (d) Administer anti-tetanus prophylaxis.
   (e) Antibiotics as indicated.
   (f) Analgesia: opiates as indicated.
   (g) Administer ibuprofen 400 mg orally every 12 h up to maximum of 2400 mg/day.
4. Prohibit smoking.
5. Consider use of TPA, Iloprost if the patient is at high risk for amputations and does not have any contraindications.
6. Use imaging: (99Tc) triple phase bone, SPECT/CT, +/− MRA to guide in delineation of the tissue injury and eventual surgical management.
7. Treat wounds expectantly, allow for demarcation, and treat surgically as indicated with imaging guidance.

There has been much advancement in the treatment of frostbite in recent years which allowed for improved care of the patients with frostbite. Two such adjunctive therapy are the use of thrombolytic therapy and administration of Iloprost (prostacyclin analog) [64–71]. The use of thrombolytics (tissue plasminogen activator—TPA) in the first 24 h post injury has been shown to decrease amputation rates significantly [64–66, 69]. Thrombolytics need to be delivered in specialized centers that have adequate experience with frostbite injury and can provide the appropriate monitoring to ensure success [46, 65–69]. The earliest publication in the use of Iloprost in the treatment of frostbite was in 1994 by Groechenig [70]. In subsequent publication, the use of Iloprost in frostbite has been associated in significant reduction in amputation rates in at risk digits [66, 70–72]. The key advantages of Iloprost over TPA is that it can be administered more than 24 h post injury and it is not contraindicated in trauma. The dosing of iloprost has been reported by Lindford et al. at an initial rate of 0.5 ng/kg/min and gradually increased to a maximum of 2 ng/kg/min for 6 h per every 24 h period for 2–3 days [72] and upto 5 days by Poole in Canada [71].

There are other studies in the utility of novel therapies (hyperbaric oxygen therapy [73–76] and nanogel topical agents [76–78]) for the treatment of frostbite; however, there is no conclusive data to prove them as gold standard for use in the clinical setting.

The above-mentioned therapies and medical interventions are key in the treatment of frostbite and can reserve surgical intervention for when absolutely indicated. The surgical management of frostbite is time dependent allowing for demarcation of the soft tissue necrosis. If amputations are required, the use of bone scan with SPECT/CT can more accurately guide the planning of the definitive procedure (level of amputation).

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Long-Term Sequelae of Burn Injury: Current Understanding of Pathophysiology, Therapeutic, and Rehabilitative Options with an Emphasis on Hypertrophic Scarring and Laser Therapy

Daniel Popp, Ludwik K. Branski, and Lars-Peter Kamolz

1 Introduction

The chances of survival after a major burn injury have constantly increased over the past decades and further decreases in mortality rates seem to be out of reach [1]. Recent data shows that 96.8% of all patients treated in a US burn center survive [2]. However, many survivors suffer from disfiguring scarring, life-long physical disabilities, and adjustment difficulties. Focus has shifted more and more attempts to improve long-term outcomes with recent advances in discovering underlying mechanisms, treatment of scars, and early rehabilitation.

In addition to recent improvements in burn care, another important aspect is prevention of burn injuries, especially in high-risk groups and vulnerable populations such as young children and adolescents, disabled, or the elderly [3]. Given the fact that 73% of all burn injuries that require burn center treatment occur at home [2], education of the public and of specific groups could help decrease the overall number of burn victims, and decrease the number of patients with major disabilities that are unlikely to be reintegrated into society and economy due to devastating long-term sequelae.

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This chapter focuses on the long-term outcomes after a severe burn injury. We emphasize one of the most relevant topics in burn rehabilitation: hypertrophic scarring, its treatment with laser therapy including practical guidance, and place them in context of the current literature.

2 Hypermetabolic Response and Long-Term Sequelae of Burn Injury on Organ Systems

2.1 Hypermetabolic Response to Burn Injury and Its Long-Term Effect on Muscle, Bone, and Glucose Metabolism

Severe burn injury leads to a **pathophysiological response** that affects almost every physiological system within the body. Hallmarks of that response are hypermetabolic stress (increased metabolic rate) with skeletal muscle catabolism (burn-induced muscle cachexia), and insulin resistance (stress-induced diabetes). This **hypermetabolic state** affects skeletal muscle-, bone-, glucose-, and lipid metabolism as well as the cardiovascular- and immune system and has been shown to persist for up to 3 years [4].

Muscle loss, strength, and cardiopulmonary capacity: After severe burn injury, skeletal muscle (depot of lean body mass) is the main endogenous source for amino acids that are required for production of acute phase proteins and wound healing. As a result, loss of lean body mass occurs after a major burn injury and aggressive nutritional support can only attenuate it partially [5]. This also has functional relevance since lean mass correlates directly with skeletal muscle function [6]. Muscle strength and cardiopulmonary exercise capacity are typically impaired in burned children and in adults compared to non-burned individuals for many years after the injury. Also pulmonary function has been shown to be reduced for up to 7 years after burn [7].

Bone: Severely burned children can be at an increased risk for fractures than their non-burned peers [8]. The exact mechanism that leads to reduced trabecular bone mass for at least 2 years after burn is not yet fully understood. However, resorptive cytokines, elevated endogenous glucocorticoid levels, oxidative stress, and immobilization seem to play an important role in mediating reduction of bone formation and bone resorption, with the result of bone net loss. It is also unclear if this leads to early osteoporosis later on [9].

Insulin resistance and glucose intolerance, and as a consequence hyperglycemia in the acute phase after burn contribute to poor wound healing, skin graft failure, and respiratory tract infections. In severely burned individuals, endogenous glucose production of the liver (central insulin resistance) is increased. At the same time, the ability to store glucose in skeletal muscle is reduced (peripheral insulin resistance). As a result, patients have abnormal high blood glucose levels that can last for up to 3 years after burn [10]. This exacerbates loss of lean body mass and patients might be at risk for developing diabetes.

Long-term effects of temporary hyperglycemia in burn patients are currently unknown; however, glucose levels are usually targeted to be in the range of 90–140 [11]. Treatment modalities for glucose level control are discussed in Sect. 3.1.

2.2 Cardiovascular Response

After a major burn injury, the reaction of the cardiovascular system is complex. The cardiac response to the altered sympathomimetic response of the beta-adrenergic system is problematic and leads to an imbalance of oxygen demand and supply [12]. Contractility is reduced directly after burn due to increased release of antidiuretic hormone (ADH) [13]. Circulating pro-inflammatory cytokines such as TNF-α are impacting intracellular calcium currents and thus account for inducing cardiomyocyte apoptosis and further decreasing myocardial contractility [14]. Furthermore, massive plasma losses after major burn are likely to lead to hypovolemia with hypoperfusion and subsequent central organ ischemia, including acute myocardial and renal ischemia [15]. Elevated pulmonary artery resis-

tance caused by inhalation injury or pulmonary edema typically lead to right ventricular dysfunction [16]. Overall, these mechanisms lead to impaired relaxation, contractility, and reduced compliance of mainly the left ventricle [17, 18]. Compensation for the resulting reduced cardiac output occurs by increasing the heart rate, leading to increased demands of oxygen further leading to bilateral cardiac dysfunction [17, 19, 20].

Cardiac dysfunction is not only a problem during the acute phase, but persists at least for 2 years after burn [21]. A more recent study found that adolescents and young adults who were burned as children demonstrate cardiac abnormalities as long as 12 years after burn. In particular, they found myocardial fibrosis, systolic and diastolic dysfunction, and reduced exercise capacity compared to a non-burned control group. These findings indicate that burn injury leads to tissue remodeling in the heart [22]. Ongoing research aims in discovering underlying mechanisms.

2.3 Effects on the Pulmonary System

Inhalation injury contributes substantially to mortality in burn patients [23]. The pathophysiologic changes in the acute phase are well studied; however, only a few long-term studies exist. Furthermore, comparison of outcomes and measurements remains difficult because burn injury itself affects muscle mass and function, while scarring can lead to reduction of chest wall elasticity. Additionally, a consensual grading system for inhalation injury has not been developed [24].

Lung injury and subsequent long-term outcomes may be attributed to different mechanisms: inhalation injury and inhaled toxins, long-term mechanical ventilation, the systemic inflammatory response syndrome (SIRS), hypermetabolism, pneumonia, or sepsis [25].

For at least 6 months after smoke inhalation injury, airways are hyperactive and bronchospastic, causing patients to develop a productive cough. Elevated levels of inflammatory cytokines are typically found in serum, but elevated levels can also be seen in bronchioalveolar lavage [26]. Both, obstructive, and restrictive patterns, either alone or in combination, can occur after a burn injury, whereas it is more frequent in patients with concomitant inhalation injury [27]. Peak oxygen uptake (VO_2 peak) and time to fatigue is reduced in severely burned patients when tested by an incremental exercise test 5 years after burn and compared to healthy controls [28]. Studies in severely burned children have shown that although they can reach the same endurance levels as their healthy peers, their effort is greater and their respiratory system is more challenged [29]. In summary, pulmonary function and aerobic capacity are impaired for several years after burn, both in adults and children. However, burned children with inhalation injury have comparable long-term quality of life outcomes as burned children without inhalation injury [30]. The effect of exercise programs on cardiopulmonary function are discussed elsewhere in this chapter.

2.4 Long-Term Effects of Kidney Dysfunction

Acute kidney injury (AKI) is strongly associated with high mortality, in particular if it develops in the early postburn phase [31]. Patients who need an increased number of operations, receive nephrotoxic drugs, receive a high cumulative fluid balance early on and develop sepsis are at an increased risk for kidney injury [32].

The overall prevalence of acute kidney injury is approximately 25% with a median mortality of 35%. Renal replacement therapy is required in about 1–3% of burn patients with acute kidney injury. Unfortunately, these patients have a mortality rate of up to 80%. Furthermore, AKI is associated with the need for mechanical ventilation and a longer intensive care unit stay [33, 34].

AKI is thought to be a complex problem that affects the whole body on a metabolic, endocrine, and overall organ function of all organs that can persist even after renal recovery. The mechanisms of the so-called organ crosstalk include elevated vascular permeability, changes in gene

transcription, inflammatory cytokines, apoptosis, and cell recruitment [35, 36]. Preventing AKI therefore will not only reduce prevalence of chronic kidney dysfunction and its side effects but potentially has an effect on overall long-term outcomes.

2.5 Effects on the Liver

The liver is the major organ modulating the acute phase response via various pathways and thus affecting the inflammatory—and immune response, which has a great impact on recovery and mortality [37, 38].

Liver injury is correlated with the severity of the burn and is usually present to a variable extent in burn patients. Occurrence of liver and heart failure together is common and is associated with a longer hospital stay [39].

Fatty infiltration of the liver is a common finding in burn patients and is reversible [40]. Yet, in non-survivors fatty liver infiltration is associated with liver failure and sepsis, indicating an important role in the acute postburn phase [41].

Liver dysfunction is present immediately after burn, it typically peaks 2 weeks after burn and persists for 4–12 weeks. Mortality is also higher in patients who develop liver dysfunction than in those without [42]. In a study by Jeschke et al. [40], liver weight and size were massively elevated for up to 12 months postburn and hepatic protein synthesis was affected for up to 9 months. In particular, patients had reduced serum levels of albumin, pre-albumin and transferrin, and elevated acute phase protein levels. Serum AST and ALT levels, markers of hepatocyte damage, remained significantly elevated for up to 4 weeks after burn and returned to normal levels afterwards.

It is known that hepatocytes undergo both, necrosis and apoptosis. The mechanisms however have not been fully discovered yet. Hypoperfusion or ischemia-reperfusion and circulatory pro-inflammatory cytokines are considered leading to apoptosis and enzyme release. Hepatomegaly in burn patients is caused by two mechanisms: intrahepatic steatosis and edema. Fluid overload lasts for only about 1 week after resuscitation. Hence, over-resuscitation seems not to be the cause for edema formation [40, 43].

The liver also plays a central role in glucose metabolism postburn, as it releases more glucose than the body is able to utilize (central insulin resistance), as discussed above.

2.6 Mental Health and Pain

2.6.1 Acute- and Post-traumatic Stress Disorder

Preexisting psychiatric disorders are very common in burn patients and increase the risk for sustaining a burn either directly by leading to self-inflicting burns and suicide attempts, or indirectly increasing the risk (e.g., impulse control disorder, personality disorders, substance abuse including smoking, major depression). Those patients also have an increased risk to develop psychiatric problems after the burn [44]. The two most common psychiatric problems after a burn are Acute Stress Disorder (ASD) and Post-Traumatic Stress Disorder (PTSD). Both have many criteria in common, with the most important difference being time of occurrence. The cut-off point is 1 month after burn. Adults more frequently develop PTSD than children, with a prevalence ranging between 3% and 35% at 2 years postburn. That number decreases to 7–25% 3 years postburn [45] and is 2–19% in children [46, 47].

Patients that develop PTSD after a trauma are highly likely to develop psychological comorbidities such as anxiety, depression, substance abuse, and in particular suicidal behavior in adults [48, 49]. Especially children can develop issues in regard to mood and sleep as well as conduct, attention, and learning problems [50]. In addition, burn survivors in particular suffer frequently from adjustment difficulties and disturbed body image due to hypertrophic scars and disfigurement. Patients typically experience flashbacks or nightmares of the trauma, apart from various symptoms that can overlap with other psychiatric disorders [51]. Good relationships and social surroundings, participation in

leisure activities as well as positive expectations of the future are helpful in preventing PTSD [45]. Tools for assessment of PTSD can be found at https://www.ptsd.va.gov/professional/assessment/all_measures.asp.

Support groups are an important way to help burned individuals recover and often accompany them for life. They offer a variety of support for all age groups, and especially provide mental support. More detailed information can be found at the websites of The Phoenix Society and Burn Model Systems at https://www.phoenix-society.org and https://msktc.org/burn.

2.6.2 Pain

Burn patients often experience pain that can potentially be limiting and disabling. In fact, it is their number one complaint. An increase in the severity of pain and/or localizations correlate with depression and anxiety. But more interestingly, if symptoms of anxiety or depression are present, patients experience more severe pain [52]. Adequate pain control not only reduces pathophysiological stress responses with reduced production of cortisol and catecholamines, it also reduces the likelihood for the development of post-traumatic pain symptoms [53, 54]. Furthermore, reduced or abnormal sensibility does not only occur in the burned or grafted areas, but also in non-burned regions of the same patients. Thus, changes in the central nervous system are suggested [55].

2.6.3 Post-traumatic Growth

In modern trauma therapy, the focus is not only on reducing adverse effects, but also on supporting psychologic development from the traumatic event. Post-traumatic growth (PTG) is the "positive psychological change that results from a struggle through a life-altering experience" and in adult trauma survivors consists of "greater appreciation of life, improved interpersonal relationships, greater personal strength, recognition of new possibilities in one's life course, and spiritual or religious growth [56, 57]." To gain PTG, the trauma needs to be strong enough to significantly affect the patient's world view, but must not be so detrimental that the patient cannot recover. Notably, it is possible that PTG and distress are present at the same time, and studies have shown that distress is necessary initially for growth to happen later in the recovery phase [58]. Several factors have been identified as predictors for PTG; however, ultimately problem-focused coping and cognitive processing can be actively therapeutically addressed [59].

2.7 Long-Term Effects on the Skin: Hypertrophic Scarring

2.7.1 Pathophysiology of the Hypertrophic Burn Scar

Hypertrophic scarring (HTS) is currently one of the most challenging problems after burn injury, if not *the* most challenging. With a prevalence of approximately 70% [60], it is a massive burden to burn patients and affects them physically, functionally, and psychologically and is therefore the most important issue for reintegration into society.

Hypertrophic scars and keloids are the result of aberrant wound healing, with greatly enhanced fibroblast activity and deposition of collagen. HTS consist of thin collagen fibers that are typically organized in nodules with presence of α-smooth muscle actin (α-SMA), whereas in keloids collagen fibers are thickened and hyalinized [61]. Due to their different pathophysiologic mechanism, keloids grow over a long period of time and can occur without an obvious trigger. They grow beyond the border of the original wound and exhibit a high recurrence rate after surgical excision. HTS on the other hand develop within a few weeks after the skin injury, remain within the borders of the wound, tend to regress to a certain extent over time, and have typically low recurrence rates [62].

In this chapter, we focus on the current understanding of pathophysiology, development, characteristics, and current treatment options of the most relevant scar type developing after burn injury: the hypertrophic scar.

2.7.2 Key Aspects of Hypertrophic Scar Development

The deeper the burn wound, the longer it takes to heal [63]. As a result, deep burn wounds that take longer than 3 weeks to heal are significantly associated with higher risk for developing HTS [64, 65].

The composition and architecture of the extracellular matrix (ECM) is drastically changed, fibroblasts and keratinocytes display increased profibrotic properties and profibrotic cytokines are upregulated and expressed for a prolonged period of time. Collagen production and collagen degradation, both are impaired. In normal wound healing, immature type III collagen is gradually replaced by mature type I collagen, and collagen bundles are organized parallel to the skin surface. In HTS however, type III collagen is proportionally increased and the bundles are highly disorganized [66]. Elastin, important for skin elasticity, is not present in HTS for several years after burn [67].

Nodules, consisting of highly unorganized, immature collagen, small vasculature and large amounts of mucopolysaccharide are seen histologically. These pathognomonic nodules are sharply delineated from surrounding scar tissue, which are mostly composed of similar materials but demonstrate features of more mature scars (i.e., parallel orientation of collagen fibrils) [67].

2.7.3 Proteoglycans and Glycoproteins

Another feature of HTS is elevated turgor and volume due to elevated glycosaminoglycan levels that lead to a hyperhydrated state. Decorin, a small leucine-rich proteoglycan (SLRP), responsible for collagen fibril organization, is significantly downregulated in HTS. It also controls profibrotic cytokines (TGF-β, PDGF) and several growth factors (epidermal growth factor EGF, insulin-like growth factor 1 IGF-1) by antagonistically binding and downregulation, what is disturbed in HTS [68].

2.7.4 Cellular Mechanism Involved in HTS

Deep dermal fibroblasts also play a role in HTS development. They are larger and exhibit the following features compared to superficial fibroblasts: increased collagen and decreased collagenase and decorin production, with increased production of inflammatory cytokines, namely transforming growth factor-β (TGF-β) and platelet-derived growth factor (PDGF) [69]. It is still unclear whether superficial fibroblasts are simply destroyed by injury and therefore cannot initiate the wound remodeling process or if cytokine stimulation leads to selective proliferation of deep dermal fibroblasts [70].

Myofibroblasts are responsible for wound contraction in the normal wound healing process. In HTS, they express large amounts of alpha α-smooth actin—similar to smooth muscle cells—and are the main factor responsible for the extensive contractions after burn injury [71]. Mechanical stress increases myofibroblast activity, prevents apoptosis of myofibroblasts [72], and leads to excessive accumulation of extracellular matrix. Yet, in burn patients HTS paradoxically occur also in areas minimally exposed to mechanical stress.

Hyperproliferative keratin phenotypes produced by activated keratinocytes have been identified in HTS tissue. These activated keratinocytes suggest disturbances at an epidermal-mesenchymal level [73] and may have negative impact on re-epithelialization.

2.7.5 Cytokines

Several cytokines play an important role in HTS development. TGF-β, for example, is a strong proliferative cytokine that interacts with many other cytokines and is highly upregulated in the serum and in wounds of burn patients. It plays an essential role in many wound healing processes. Of notice, one isoform, namely TGF- β_3, has antifibrotic properties and plays a role in the remodeling phase, which could be a potential therapeutic target [74].

2.7.6 Summary

Despite many theories to explain the mechanism of hypertrophic scar formation, it is still poorly understood and subject to extensive ongoing research.

3 Therapeutic Approaches of Long-Term Burn Sequelae

3.1 Pharmaceutical Treatment Options and Investigational Drugs

Recombinant growth hormone (rhGH) has been shown to lead to faster burn wound closure and donor site healing in children and adult burn victims [75]. At our center (Shriners Hospitals for Children and UTMB, Galveston), Branski and colleagues demonstrated numerous beneficial long-term effects (for up to 2 years) after a yearlong rhGH administration in severely burned children. Hypermetabolism was attenuated, lean body mass increased, body fat decreased, and cardiac output had decreased [76].

When administered acutely in critically ill adults, it led to increased morbidity and mortality [77]. Therefore, patients should be monitored closely for possible side effects, in particular hyperglycemia and hypercalcemia. Another disadvantage is the need for daily subcutaneous injections. The effects of long-term growth hormone administration (for 9 months after burn) on cardiac function, muscle strength, cardiopulmonary exercise function, after burn scarring, and overall safety in adult burn survivors are currently under investigation.

Oxandrolone, an orally administered anabolic steroid with a better side effect profile than rhGH, has been shown to attenuate hypermetabolism and lead to an increase in lean body mass, muscle strength, and growth in height in severely burned children, when administered for 1-year postburn [78], with even greater increases in bone density when administered for 2 years [79]. In adult burn victims, long-term data is lacking; however, beneficial effects have been documented for the early rehabilitative phase [80]. Although no liver failure has been reported, transaminases need to be monitored closely due to risk of abnormal liver function.

The non-selective β-adrenergic antagonist **propranolol** effectively and safely attenuates the hypermetabolic response and reduces heart rate and resting energy expenditure after burn [81, 82]. It has been shown that it not only blunts acute skeletal muscle loss [83], but more recently it also helps regain muscle mass in the early rehabilitation phase when administered for 1 year after burn [81].

The **combination of oxandrolone and propranolol** administered for 1 year after burn injury was shown to be safe and seems to have positive effects on hypertrophic scars and physical and psychological outcomes in children. Improvements could be shown 2 years after burn and therefore is suggested to be considered a treatment option in severely burned children [84].

Several therapies have been investigated to treat **bone loss**: Early intravenous administration of the bisphosphonate pamidronate successfully prevented loss of total body and spine bone mineral content (BMC) in the short term compared to placebo as well as 2 years postburn where BMC was still increased in the spine but no difference in whole body BMC was seen. Oxandrolone, given for 1 or 2 years has the potential to improve BMC as well as accelerate growth in height in burned children [79, 85]. Vitamin D substitution has not been shown to improve loss of BMC postburn to date, however improved serum Vitamin D levels in adults and reduced fracture incidence in children were seen [86, 87].

Several strategies exist for attaining **glucose control** to improve insulin sensitivity and to reduce skeletal muscle catabolism. With insulin therapy, glucose control can usually be maintained, however puts the patient at risk for hypoglycemia, and therefore has to be monitored closely [88].

An alternative treatment option is the oral biguanide **metformin**, with low risk for hypoglycemia [89]. **Fenofibrate**, a drug of the fibrate class, was shown to attenuate insulin resistance. However, data is too sparse yet to recommend it as standard treatment [88].

3.2 Physical Exercise Therapy

Positive effects on muscle strength, lean body mass, and peak cardiovascular exercise capacity during the rehabilitative phase after major burn injury in children [90, 91] and adults [92] have been shown after different exercise protocols. These effects seem to be even stronger if in addition if the growth hormone oxandrolone (0.1 mg/kg/day) is administered for 1-year postburn [93]. Also the combination of exercise with the non-selective β-adrenergic blocker propranolol (4–8 mg/kg/day, depending on resting-heart rate) appears to have beneficial effects on cardiovascular exercise capacity (VO_2 peak) in burned children [94]. More recently, the combination of the two drugs has been shown to add positively to exercise training to gain muscle strength and improve protein turnover during the early rehabilitative phase [95]. 12 weeks of a combined aerobic and resistance exercise training program was shown to be beneficial in severely burned children with improvements in peak oxygen uptake (VO_2 peak) and pulmonary function [96].

At our institution (Shriners Hospitals for Children and UTMB, Galveston), exercise protocols are in place as standard of care to help burn victims restore lean body mass, muscle function and to improve cardiopulmonary capacity. Future research should focus on objectively measurable exercise parameters to develop adequate exercise programs also for adult burn survivors since there is great inconsistency between burn centers and lack of awareness of the importance of such programs, as the survey of Diego and colleagues has shown [97]. It should be pointed out that no study has shown that beneficial effects of exercise training last beyond the rehabilitative phase. Nonetheless, as with the non-burn population, it is essential that physical exercise becomes an integral part in a burn survivor's life to be beneficial long term.

3.3 Scar Therapy

Apart from the stigma and unpleasant aesthetic appearance that accompanies hypertrophic burn scars, burn survivors suffer from severe pruritus, neuropathic pain, and contractures that often limit range of motion [98, 99]. The most important scar treatment is their prevention. Early excision, the avoidance of skin grafts—if possible, according to burn depth—and early pressure garment therapy are key. If a scar has formed despite preventive therapy, the most effective and important therapy is reconstructive surgery. This is discussed in detail elsewhere in this book.

A holistic approach is usually applied to prevent and treat hypertrophic scars, ranging from traditional conservative therapies, such as compression garments, silicone sheets or gels, physical therapy, intralesional injection of corticosteroids, or 5-fluorouracil. Effectiveness of these extensively used conservative methods has been proven empirically and are widely acknowledged legitimately as standard of care; however, to date little scientific evidence exists supporting their use due to the fact it is difficult to conduct adequately powered randomized clinical trials. Side effects can occur [62, 100–102], however in general they are quickly reversible once the treatment is stopped.

Pressure garments are in use for the prevention and treatment of HTS for over half a century and are still considered as standard basic treatment. They are worn for almost 24 h a day for at least 6 months after burn. The pressure achieved ranges between 15 and 40 mmHg [103, 104]. A recent animal study suggests starting pressure therapy immediately after skin graft take might be beneficial [105]. Even though in many cases it is difficult to attain sufficient pressure to the affected area and due to comfort issues, lack of compliance can occur, pressure garments are still to date considered standard treatment for burn scars.

Silicone sheets are usually worn for at least 12 h/day for several months, beginning therapy 2 weeks after wound healing. The mechanisms of action of silicone gel sheeting are occlusion and therefore increased skin hydration and electrical charge changes possibly due to the silicone molecule. To prevent maceration, sheets have to be removed intermittently to let the skin dry [101]. Side effects such as rash, pruritus, contact dermatitis, and dry skin can occur [106]. The combination of both, pressure garments and silicone

sheets, exhibits increased efficiency over one treatment alone [102].

The combination of intralesional injections with **Triamcinolone (TAC)** and **Fluorouracil (5-FU)** is the most effective regimen. It is more effective over each single treatment alone and has also less side effects, like skin atrophy or telangiectasia. As standard regimen 0.1 mL 40 mg/mL concentrated TAC mixed with 0.9 mL 50 mg/mL concentrated 5-FU is recommended. Scars should be treated weekly for at least 8 weeks. The dose administered should not exceed 2 mL in total per session or 0.5 mg/cm^2 [102].

Medical needling is indicated for large burn scar plates that cannot be treated with excision and flaps. A roller with 1–3-mm-long needles is typically rolled in vertical, horizontal, and diagonal directions over the scarred area. The small needles penetrate the papillary and reticular dermis causing mechanical micro injuries without thermal injury or necrosis as compared to other scar resurfacing methods. This induces new collagen and elastin formation and results in thinning of dermis, thickening of the epidermis, increase in non-inflammatory cytokines, and improvement of scar texture with a very low risk for hypo-/hyperpigmentation and scarring. The procedure can be performed under local- or short systemic anesthesia. Currently, there are fully automated devices on the market which are adjustable in speed and penetration depth; however, the principle remains the same. Noninvasive medical needling is also used for intralesional delivery of topical drugs, or can be used in combination with radiofrequency [107, 108]. Figure 1 shows pre- and post-interventional results.

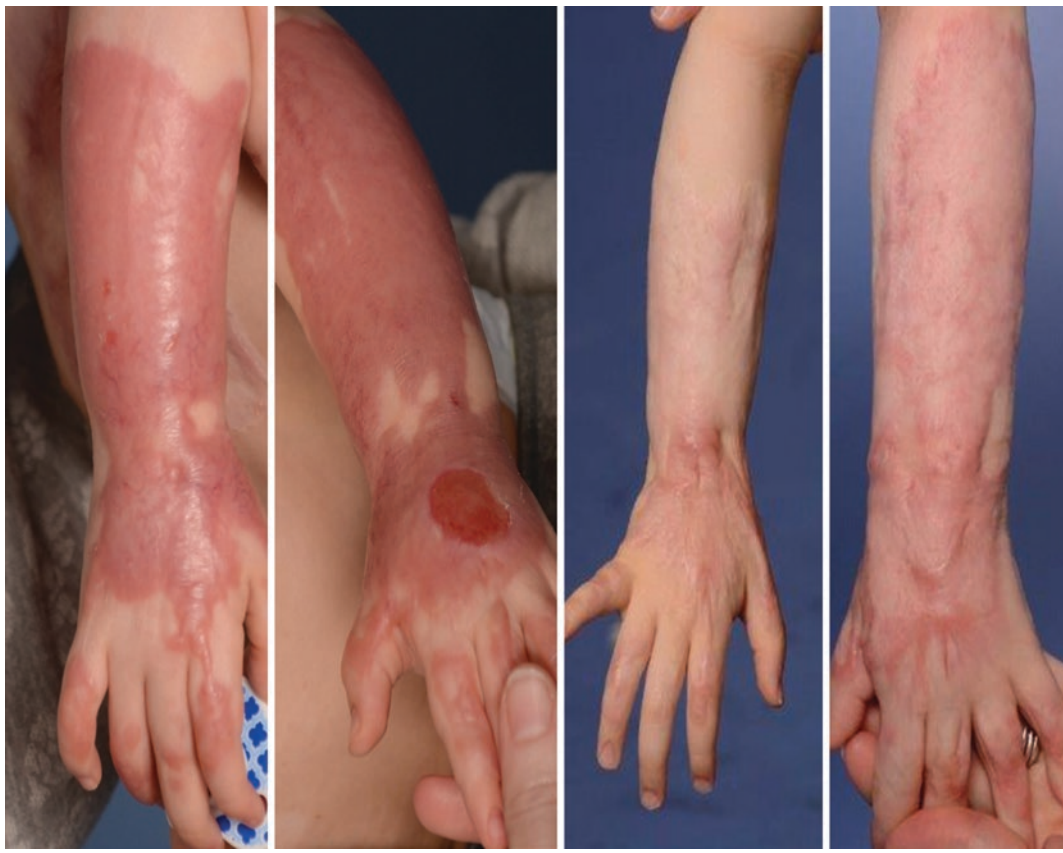

Fig. 1 Medical needling results. Left: Hypertrophic scar area localized on the right cheek and neck, preoperatively. Right: Result 3 months after medical needling. The scar texture has significantly improved without changes in pigmentation

Autologous fat grafting for reconstructive or aesthetic purposes became popular over the recent years. Basic science studies have shown that regeneration of all three layers of the skin is possible with autologous adipose-derived stem cells [109]. This seems to be of great benefit in particular for the treatment of burn wounds. Studies in burn patients have shown that it supports restructuring of collagen, improvement of pigment disorders and overall scar texture. Even though level of evidence is low and more clinical studies are required [110], autologous fat grafting is a promising therapeutic option for the treatment of burn scars, especially in combination with other therapies.

Laser therapy has become widely accepted as a major modality for the treatment of burn scars, especially with growing evidence of its effectiveness over the recent years [100, 111]. Attenuating the scar both aesthetically and functionally and to reduce pain and itching are the ultimate goals. Laser therapy can be used alone or in adjunct prior to surgery to soften the scar and improve outcomes.

3.3.1 Laser Types

Different types of lasers target a specific chemical entity known as a chromophore. Laser energy of a specific wavelength is absorbed by the three main chromophores melanin, hemoglobin, intra- and extracellular water. Penetration depth is dependent upon the amount of energy used [112].

Mechanistically, it has to be distinguished between ablative/non-ablative and fractional/non-fractional lasers. **Non-ablative lasers** use lower temperatures around 50–70 °C, which lead to coagulation of proteins and collagens, respectively. Whereas **ablative lasers** use temperatures greater than 100 °C, which cause tissue vaporization, surrounded by a thermal coagulation zone [113].

Fractional ablative laser therapy was developed to overcome side effects related to non-fractional ablative lasers and was first introduced in 2004 by Manstein and Anderson, who termed it fractional photothermolysis [114]. Fractional lasers split the laser beam into many microbeams, leading to hundreds to thousands of small micro injuries, called microthermal treatment zones (MTZ). Ultra-fast pulsed laser beams produce tissue ablation while significantly reducing heat deposition, and therefore causing less collateral damage. The spared surrounding tissue allows for a rapid wound healing response (re-epithelialization after 1-day post treatment), neocollagenesis, and tissue remodeling [115, 116].

Although a huge variety of different lasers have been studied for the treatment of hypertrophic burn scars, ablative fractionate lasers (AFLs) and pulsed dye laser therapy (PDL) seem to be the most beneficial.

The most frequently used laser for the treatment of hypertrophic burn scars are the ablative fractional CO_2 lasers and erbium:YAG (er:YAG). At our institution (Shriners Hospitals for Children and UTMB, Galveston), we use the fractional CO_2 laser, which we have extensive experience with. The CO_2 laser targets water in abnormal collagen up to 4 min below the surface. Figure 2 shows results of CO_2 laser therapy.

3.3.2 Laser Effects and Side Effects

The main effects that can be accomplished with CO_2 laser are a reduction of scar thickness, increased scar elasticity, improvement in surface texture and firmness, improvement in scar pigmentation (hyper- and hypopigmentation), dermal restructuring—reduction of TGF-β1 expression, increase of collagen Type I and III, thickening of epidermis, and last but not least a reduction of pain and pruritus [113, 117, 118].

Improvements in scar appearance have been shown to occur after only one single treatment [119], however usually several sessions with breaks of approximately 4 weeks to 3 months in between are required to attain a good result and can be combined with other treatment modalities like triamcinolone injections [120, 121].

Histologically, laser treatment leads to decrease in collagen bundle thickness and density in the upper dermis, and newly formed dermal papilla [122, 123]. Recent studies identified molecular effects on keratinocytes and fibroblasts [124].

Side effects/complications range from discrete to moderate erythema or edema (what usu-

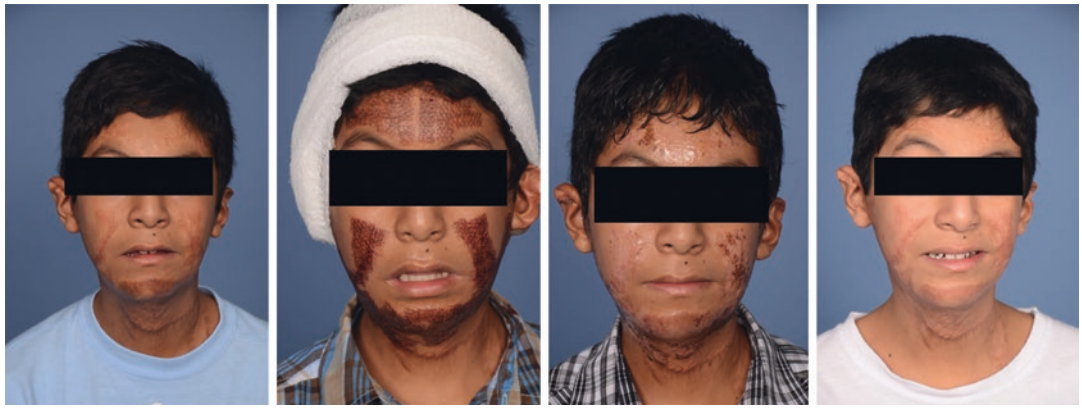

Fig. 2 CO_2 laser treatment. 11-Year-old male with hypertrophic scars with hypo- and hyperpigmented areas 2 years postburn. Left to right: Pre OP, 1 day post OP, 6 days post OP, 3 months post OP

ally resolves in 7–10 days), hyper- or hypopigmentation, post-inflammatory hyperpigmentation (PIH), pruritus or imprints from the laser-grid. Blistering is more common after PDL, whereas CO_2 lasers cause more often postprocedural pain, which can usually be treated sufficiently with non-opioid analgesics. Darker skin types are more likely to develop hypopigmentation or blistering. Overall, adverse events are rare and it can be considered a safe procedure if applied correctly [125, 126].

3.3.3 Laser Therapy: Practical Guidance

Treatment should not begin no less than 6 months after wound healing is complete and the scar has matured; however, expert's opinions vary widely. Successful results have also been accomplished with older burn scars of up to 7–23 years postburn [122, 127].

Laser selection is based on the following criteria: dyschromia (i.e., erythema, hypo- or hyperpigmentation), type of scar (hypertrophic, flat, atrophic), location (i.e., face, neck, trunk), and patient characteristics (i.e., skin type and comorbidities) [128].

We have found that the **CO_2 laser** is the most effective tool in almost all patients because it penetrates deep into tissues, necessary to treat thick hypertrophic scars. There are numerous commercially available fractional CO_2 laser units. At our institution (Shriners Hospitals for Children and UTMB, Galveston), we use the Lumenis Ultrapulse device (Lumenis, Santa Clara, CA) with various settings (ActiveFX®, DeepFX®, or SCAAR FX™). We tend to use the SCAAR FX setting for thick, hypertrophic scars, and the Deep FX setting for atrophic, papery scars. The ActiveFX is used to assist in surface changes and to treat hyperpigmentation. For immature hypertrophic burn scars, we use vascular laser settings. The underlying principle is to coagulate micro blood vessels, by targeting the chromophores hemoglobin and oxyhemoglobin, and thus eliminating the vascular supply to the scar. It also addresses localized pruritus, which can be a serious problem, especially in burned children. Historically, **pulsed dye laser** (PDL) has been used effectively for the treatment of burn scars [129]; however, it is slow and the endpoint required to see as indicator for an effective treatment is a purpuric response. At our institution, we use the Lumenis-M22 platform with different modules. One advantage of the 590 nm filter is that it has the benefits of the PDL but is faster and does not generate a purpuric response. For targeting any telangiectasia within the scar, we use the Nd:YAG handpiece. We often use the vascular laser and the CO_2 laser in the same session, with the vascular laser being used first as otherwise the effect of any vascular laser to a bleeding wound would be negligible. Figure 3 shows results of vascular laser treatment. Figure 4 summarizes frequently used laser settings.

Laser Type/Setting	Wave length	Energy	Indication	Endpoint
Ablative fractionated CO_2-Lumenis Ultrapulse	10.600nm			
SCAAR FX		60-100 mJ at 3% (100-150 mJ at 1%)	Thick, hypertrophic scars	Pinpoint bleeding
Deep FX		10-20 mJ at 10%	atrophic, papery scars	Pinpoint bleeding
Active FX		60-100 mJ at 3%, 125Hz, (5% if used alone)	Surface, hyperpigmentation	Full coverage of scar
PDL	585-595nm	7J/cm2	Erythema, pruritus	Purpuric response
M22 – Nd:YAG	1064nm		Teleangiectasia	
M22 – IPL + 590nm filter,	590nm	17J/cm2	Erythema, pruritus	

Fig. 3 Vascular laser treatment. 3-Year-old male with erythematous scars after a scald burn on both hands and forearms. Left: 7 months postburn, before treatment. Right: 16 months postburn, after two treatments with M22 laser. Additionally, the patient has been in compression garments since his wounds were closed

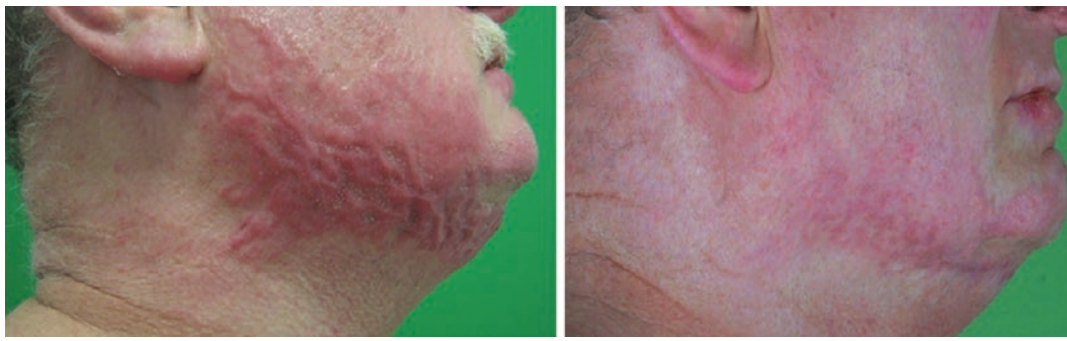

Fig. 4 Common laser/IPL Settings. *SCAAR* synergistic coagulation and ablation for advanced resurfacing, *PDL*, pulsed dye laser, *Nd:YAG* neodym YAG laser, *IPL* intense pulsed light

Pre- and aftercare: Perioperative antibiotic prophylaxis is indicated in patients with a history of infection or colonization with multi-resistant organisms. Patients with a history of herpes simplex virus undergoing ablative fractional laser treatment on the face should receive acyclovir for prophylaxis. Both are usually not necessary for non-ablative laser therapy. For patients who are likely to develop PIH, we advocate the use of Azelaic acid (15%) for its tyrosine kinase inhibitory action and have seen great results in most of our patients. Others use hydroquinone prior to laser therapy. For the actual treatment of PHI, a combination of a steroid, hydroquinone, and tretinoin can be used.

Directly after the procedure, we cool the wounds with ice packs. Lasered areas should be left open to air and kept elevated until swelling subsides. We recommend to wash treated areas twice daily with antimicrobial skin cleanser and application of hydrophilic ointment several times a day to prevent dryness and crustiness, until areas are fully epithelialized. By then, compression garments can be worn again. If pruritus occurs, hydrocortisone cream (1%) is applied locally. Sun should be avoided and at least SPF30 sunscreen lotion should be applied daily for a year when exposed after wounds have healed to support preventing PIH.

3.3.4 Conclusion

Despite its clear benefits, laser is certainly not a panacea for all burn scars. Surgical release and rearrangement of tissue is still a mainstay. However, laser therapy is definitively an essential part of any burn reconstruction program and has now become part of the standard of care. Scar management with the ablative fractional CO_2 laser is most effective in facial scars, large scar plates of the trunk, and less severe scar bands over joint surfaces, and has replaced conventional surgery in many instances.

4 Summary

Burn injury is not limited to the acute phase. On the contrary, with prolonged hypermetabolism and hypercatabolism as drivers, almost every organ system is affected. Many pharmaceutical options exist, some of them seem to be beneficial for several postburn problems at once, like muscle wasting and scarring. For the most visible organ, the skin, laser therapy has huge potential. However, well-timed surgery and proper surgical techniques are key. In order to achieve the overall goal of reintegration into everyday life, society, work place, school, etc., an individual multidisciplinary treatment plan needs to be developed and constantly adapted for each patient.

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Burn Reconstruction Techniques

Lars-Peter Kamolz, Alexandru-Cristian Tuca, and Stephan Spendel

1 Introduction

During the last decades, remarkable advances have been made in the field of burns and its understanding of molecular and cellular processes (e.g., wound healing). Patients with severe burn injuries survive more frequently. For these patients, apart from life preservation and acute burn treatment, an adequate rehabilitation and return to their former social and business life is a high priority goal [1–3].

Due to the higher survival rates after severe burns, there is an increasing number of patients requiring reconstructive intervention after burns. However, good and successful reconstructive surgery demands aside from the knowledge of different reconstructive procedures a profound understanding of skin anatomy and physiology. Further, the surgical plan should be based on careful analysis of the defects and thoughtful considerations [4].

2 From the Reconstructive Ladder to the Reconstructive Elevator

Based on concept of the reconstructive ladder by Mathes und Nahai, new advances in the understanding of the anatomy, operative techniques, instrumentation, and surgical skills have led to the concept of the reconstructive elevator: complex procedures are no longer considered as last resort procedures only. In the quest to provide optimal form and function, it is currently accepted to jump several rungs of the ladder, due to the knowledge that some defects require more complex solutions. The goal of surgical reconstruction is restoration of preoperative function and appearance. The surgeon must reconstruct the defect with tissues that is missing and which allows defect coverage with tissue of similar contour, texture, and color [5, 6].

3 The Reconstructive Clockwork

In clinical daily routine, combinations of different techniques are often applied in order to permit new reconstructive possibilities for the

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patient, but neither the reconstructive ladders of Mathes and Nahai in 1982 nor the reconstructive elevator permit a real combination of the different reconstructive procedures and techniques.

The image of interlocking wheels of a clockwork illustrates the integration of different reconstructive methods even more impressive than the conventional reconstructive ladder and elevator [7] (see Fig. 1).

4 General Principles

The most common situations after burn injuries that need corrections or reconstructions are scar contractions and hypertrophic scars which cause functional impairment. Choosing the right modality depends upon several factors, e.g., the age, gender, ethnicity, localization, or maturity of the scar (e.g., tendency for keloids or hypertrophic scar). These might help for choosing the right treatment individually from case to case.

Objective assessment of deformities and functional impairment is of utmost importance for planning the right reconstructive procedure. Formulating a realistic plan to restore the functional problems requires analysis of the physical deformities and psychological disturbance of the patient. Psychiatric, psychosocial, and physiotherapeutic cares have to be continued while a surgical treatment plan is instituted [8].

5 Indication and Timing of Surgical Intervention

Deciding when to operate a patient and to find the perfect timing can be much more difficult than taking the decision how to operate patients with burn deformities.

However, the basic principle is based on the following: Restoring bodily deformities that impose functional difficulties must precede any surgical effort to restore the appearance.

In short, a surgeon's effort must be concentrated upon restoring the deformed bodily parts essential for physical functions, if not for patient survival. In contrast, restoration of deformed regions in general can be performed in a later phase.

It is postulated that attempts to correct burn deformities should be delayed for at least

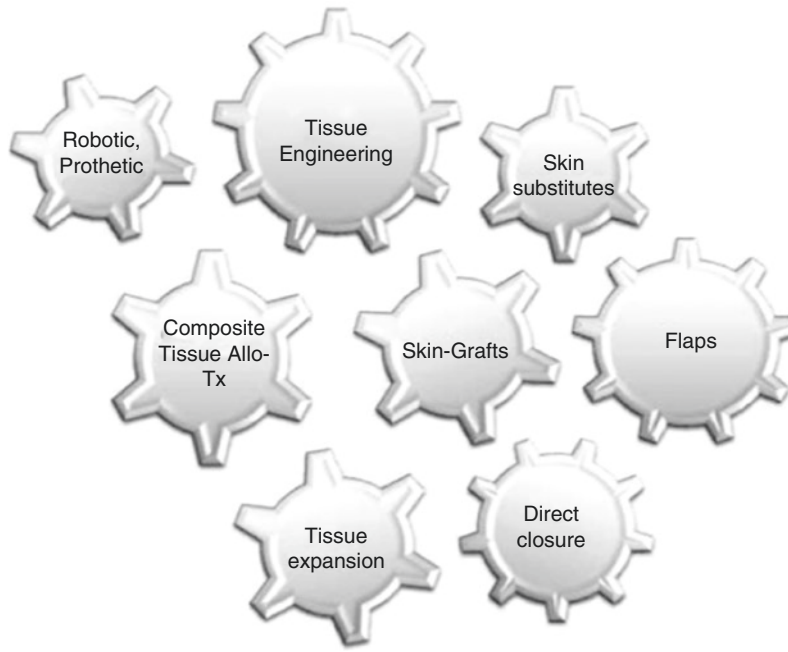

Fig. 1 The reconstructive clockwork: the interlocking wheels of a clockwork illustrates the integration of different reconstructive methods

1–2 years. During this time needed for scar maturation, an interim conservative treatment by using pressure garments and splinting is recommended to reduce scarring and to minimize joint contracture because operating on an immature scar is technically more cumbersome and will lead to a higher number of complications. It is never too late to revise a scar, but conversely, it may be too early.

6 The Techniques of Reconstruction

There are several techniques routinely used to reconstruct deformities and to close defects related to the burn trauma.

Principally, they are following techniques which will be described in more detail:

- Excision techniques
- Serial excision and tissue expansion
- Skin grafting techniques with or without the use of dermal substitutes.
- Local skin flaps
- Regional and distant flaps
- Allotransplantation
- Tissue engineering.
- Robotics and prosthesis.

6.1 Excision Techniques

Excision with direct closure of the resultant wound is the simplest and the most direct approach in burn reconstruction. It is important to determine the amount of scar tissue that can be removed so that the resultant defect can be closed directly. A circumferential incision is made in the line previously marked and is carried through the full-thickness of the scar down to the subcutaneous fatty layer. In case of a keloid, an intralesional excision might be better instead of an extralesional one in order to avoid recurrence. In order to minimize vascular supply interference along the wound edges, undermining of the scar edge should be kept to a minimum, whenever possible.

6.1.1 W-Plasty and Geometric Broken Line Closure

The *W-plasty* is a series of connected, triangular advancement flaps mirrored along the length of each side of the scar, but W-plasty, unlike a Z-plasty does not result in an overall change in length of the scar, it makes the scar less conspicuous and it disrupts wound contracture with its irregular pattern. As with all other procedures, it is helpful to mark out the planned design prior to the operation (see Fig. 2) [9, 10].

The Geometric Broken Line Closure (GBLC) is a more sophisticated scar regularization technique than the W-plasty and requires more time to execute; unlike the W-plasty's regularly irregular pattern, which results is a somewhat predictable scar pattern that can be followed by the observers' eye, the irregular irregularity of the GBLC allows maximum scar camouflage [11–13]. This is achieved by various combinations of triangles, rectangles, squares, and semicircles in differing widths and lengths along the scar (see Figs. 2 and 3).

6.2 Serial Excision and Tissue Expansion

The goal of surgical reconstruction is the restoration of preoperative function and appearance. The surgeon must reconstruct the defect with tissue of similar contour, texture, and color. Surgical excision of scars relies upon recruitment of local tissue for closure of the ensuring defect and thus adjacent skin will usually provide the best match for the defect. In areas where tissue laxity is poor or the resulting defect would be too big, tissue expansion and serial excision are useful techniques to overcome a lack of sufficient local tissue for closure. Tissue expansion allows large areas of burn scar to be resurfaced by providing tissue of similar texture and color to the defect. Moreover, it is combined with the advantage of donor site morbidity reduction. Issues and disadvantages that need to be addressed are that the technique of pre-expansion requires additional office visits for serial expansion and at least one extra surgical procedure with potential for

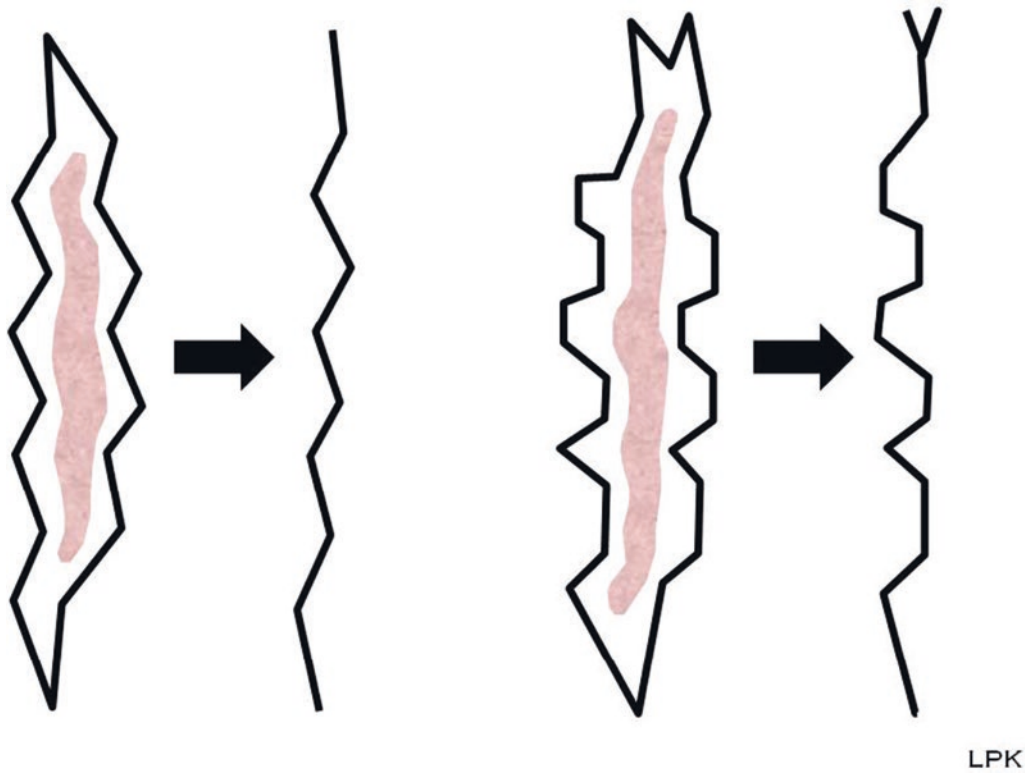

Fig. 2 W-plasty (left) and geometric broken line closure (right); (scar: pink)

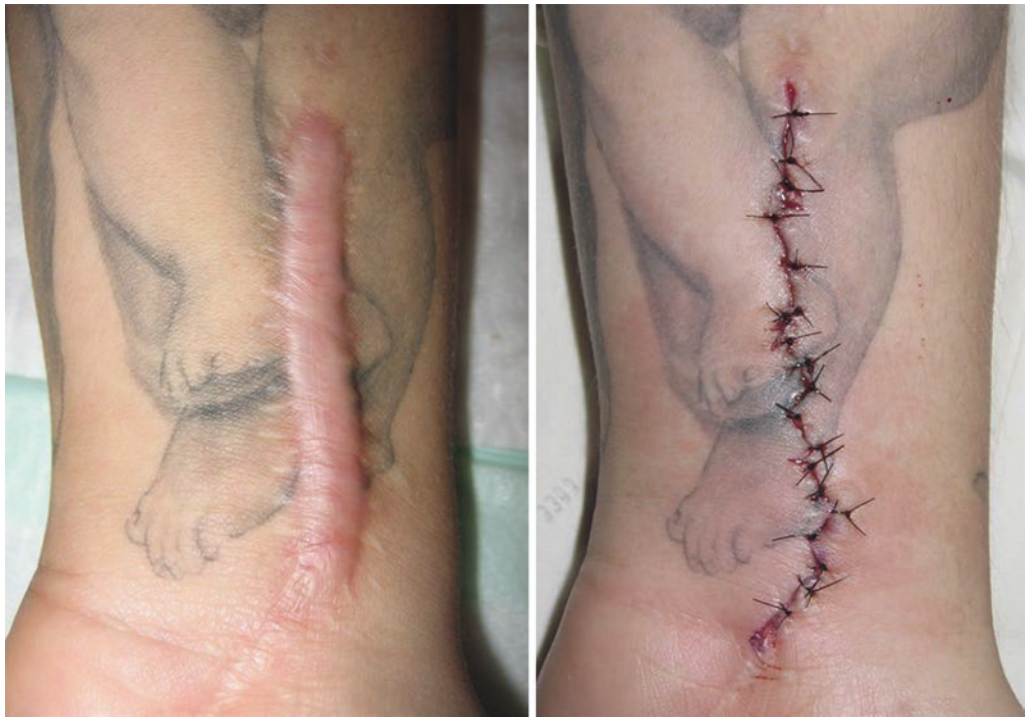

Fig. 3 Geometric broken line closure: clinical example

additional complications. A significant time period between 9 and 12 weeks for progressive tissue expansion is required. Tissue expanders are very versatile tools in reconstructive burn surgery, but still, careful patient selection, correct indications and realistic treatment concepts, large experience and well-selected surgical techniques, precise instruction of the medical staff as well as detailed and continuous education of the patients are essential [14, 15].

Serial excisions involve the partial excision of the scar together with the consecutive advancement of adjunct skin. In a series of sequential procedures, the area of scar is excised completely. The number of procedures needed depends on the elasticity of the surrounding skin and the size of scar being excised. The primary disadvantage of this technique is the requirement for multiple operations. Should more than two operations be needed, tissue expansion should be considered or evaluated as an alternative treatment option.

6.3 Skin Grafting Techniques

A skin graft in the combination with a dermal substitute—Covering an open wound with a skin graft harvested at a various thickness is the conventional approach of wound closure. A skin graft including epidermis and dermis is defined as a full-thickness skin graft, and a piece of skin cut at a thickness varying between 8/1000 of an inch (0.196 mm) and 18/1000 of an inch (0.441 mm) is considered to be a partial- or a split-thickness skin graft. The thickness of a full-thickness skin graft is quite variable depending upon the harvest region.

In case of a full-thickness skin graft, a paper template may be made to determine the size of the skin graft needed to close a wound. The skin graft is laid down to the wound bed and is anchored into place by suturing or stapling the graft onto the wound bed. A continuous contact of the skin graft with the wound bed is essential to ensure an in-growth of a vascular network in the graft within 3–5 days and thereby for the graft survival. A gauze or cotton bolster tied over a graft has been the traditional technique to anchor and to prevent fluid accumulating underneath a graft, if there is a flat and well-vascularized wound bed. In regions, which are associated with a less good take rate (concave defects; regions, which are subject to repeated motion like joints) or in patients with comorbidities, which may have an impact on graft healing, other techniques instead of the bolstering technique, are used for skin graft fixation. The use of topical negative pressure or fibrin glue can lead to better skin graft healing [16–18].

The criteria for using skin grafts of various thicknesses are mainly based on:

- The use of a thin graft is more appropriate for closing wounds with unstable vascular supplies, particularly if the skin graft donor site is scarce.
- Moreover, the quality and the presence of dermis seem to have an influence to the extent of wound contraction. The extent of contraction, which is noted if a thin partial-thickness skin graft is used, is larger than using a full-thickness graft. The presence of a sufficient dermal structure could reduce wound contracture.

Skin graft in combination with a dermal substitute—For the past several years, artificial dermal substitutes have been used in order to improve skin quality, e.g., Alloderm™, Integra™; these materials when implanted over an open wound have been found to form a layer of resembled dermis, thus providing a wound bed better for skin grafting and thereby better skin quality [19]. However, the need for a staged approach to graft a wound using this technique is considered cumbrous. Matriderm ™ is a new dermal matrix, which consists of collagen and elastin and allows a single-step reconstruction of the dermis and epidermis in combination with a split-thickness skin graft (see Fig. 4a–e) [20–22].

6.4 Local Skin Flaps

The approach using a segment of skin with its intrinsic structural components attached to cover

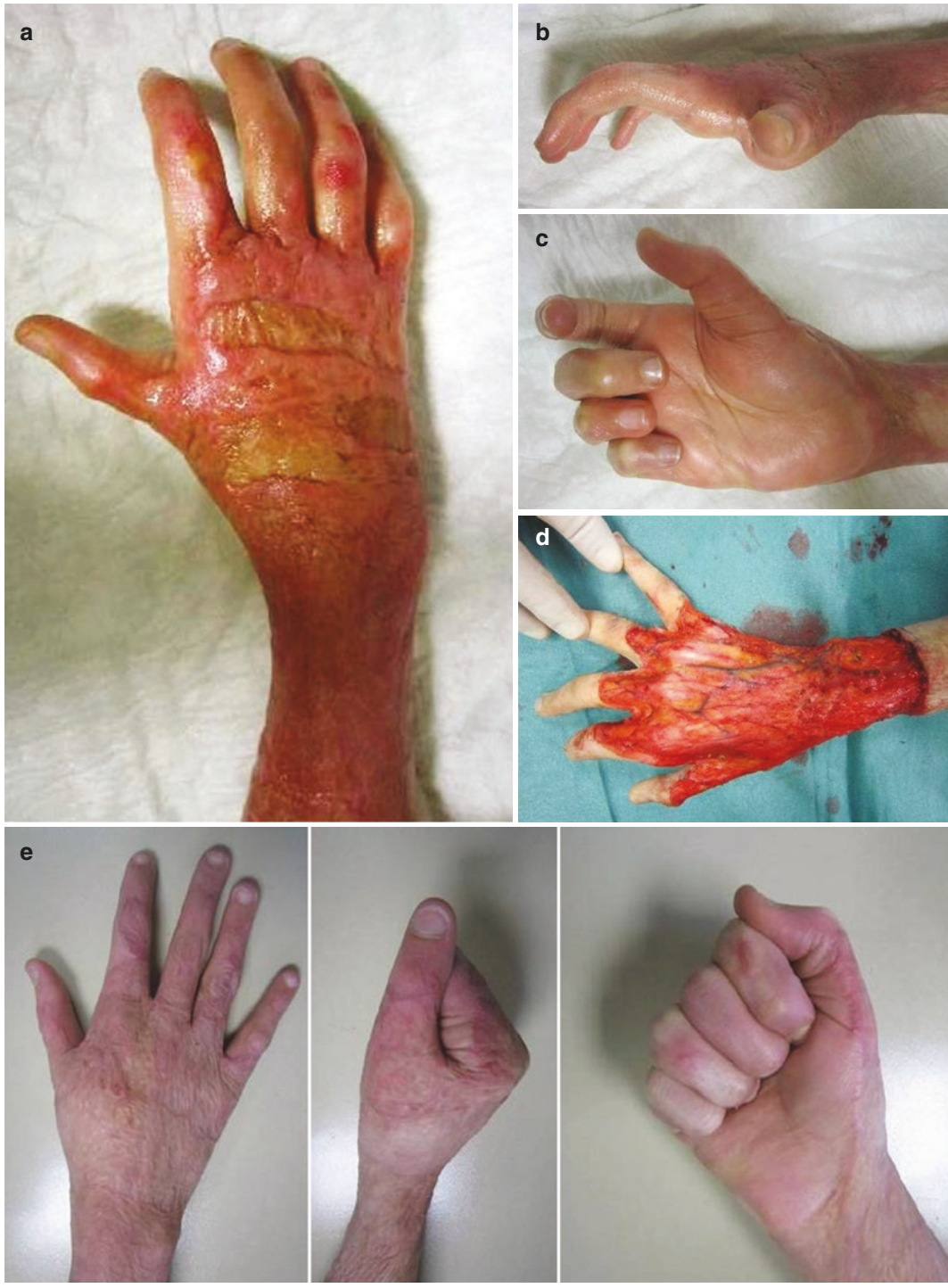

Fig. 4 (**a**) Hypertrophic and contracted scars (right hand). (**b**) Hyperextension in the MCP joints. (**c**) Flexion only possible in the PIP und DIP joints, hyperextension in the MCP joints. (**d**) Complete excision of the hypertrophic and contracted scar plate. (**e**) Late results obtained by use of Matriderm® and skin graft in a single-step procedure (6-month postoperative)

a defect follows also the fundamental principle of reconstructive surgery to restore a destructed bodily part with a piece of like tissue. The recent technical innovation of incorporating a muscle and/or facial layer in the skin flap design, especially in a burned area, further expanded the scope of burn reconstruction as more burned tissues could be used for flap fabrication.

No single flap is optimal for every scar excision. Each individual scared area must be analyzed for:

- Depth of the scar
- Tissue involved
- Availability of normal tissue for reconstruction

Based on this, the ideal flap or the combination of flaps and techniques is chosen for reconstruction.

Often used skin flaps are the Z-plasty technique, the multiple Z-plasties, the 3/4 Z-plasty technique.

Z-plasty

There are three purposes to perform a Z-plasty:

- To lengthen a scar or to release a contracture
- To disperse a scar
- To realign a scar within a relaxed skin tension line

The traditional Z-plasty consists of two constant features; first, there are three incisions of equal length—two limbs and a central incision. Second, there are two angles of equal degree—the limbs form 60° angles with the central incision (see Fig. 5). Ideally, the central incision should through the axis of the scar; alternatively, the scar itself may be completely excised with a fusiform defect acting as the central incision.

Double Opposing Z-Plasty

Two Z-plasty incisions placed immediately adjacent to one another as mirror images will produce an incision known as a double opposing Z-plasty (see Figs. 6 and 7). The advantage of this technique is that significant lengthening can be achieved in areas of limited skin availability. Ideal indication for this technique is the release web space contractures (see Fig. 8).

The *¾ Z-plasty or half-Z* used to refer the technique (Fig. 9) with one limb incision being perpendicular to the central one. The incision is created on the scar side, which creates a fissure into the scar in which a triangular flap is introduced. The length gained on the scar side is directly proportional to the width of the triangular flap.

Despite its geometric advantage in flap design, fabricating a skin flap or skin flaps for reconstruction of burn deformities is not infrequently plagued with skin necrosis. Aberrant vascular supplies to the skin attributable to the original injury and/or surgical treatment could be the factor responsible for problems. In recent years, the use of a skin flap designed to include muscle or fascia underneath has expanded further the usefulness of conventional Z-plasty and the 3/4 Z-plasty technique in burn reconstruction.

Moreover, multiple Z-plasties are often used for scar corrections (see Figs. 10 and 11).

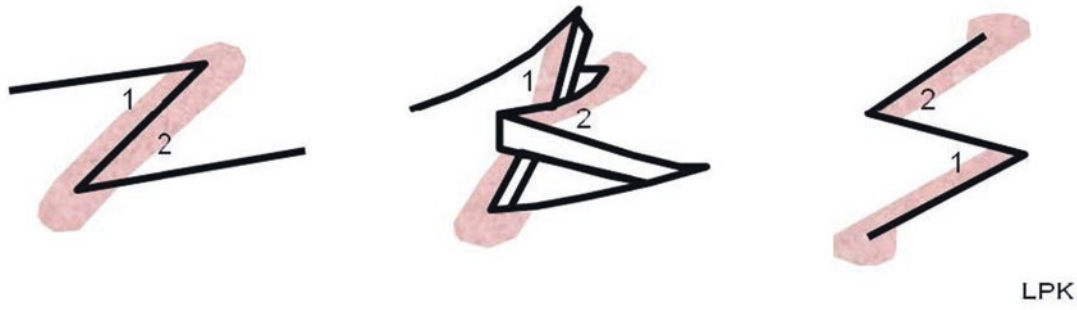

Fig. 5 Z-plasty (scar: pink)

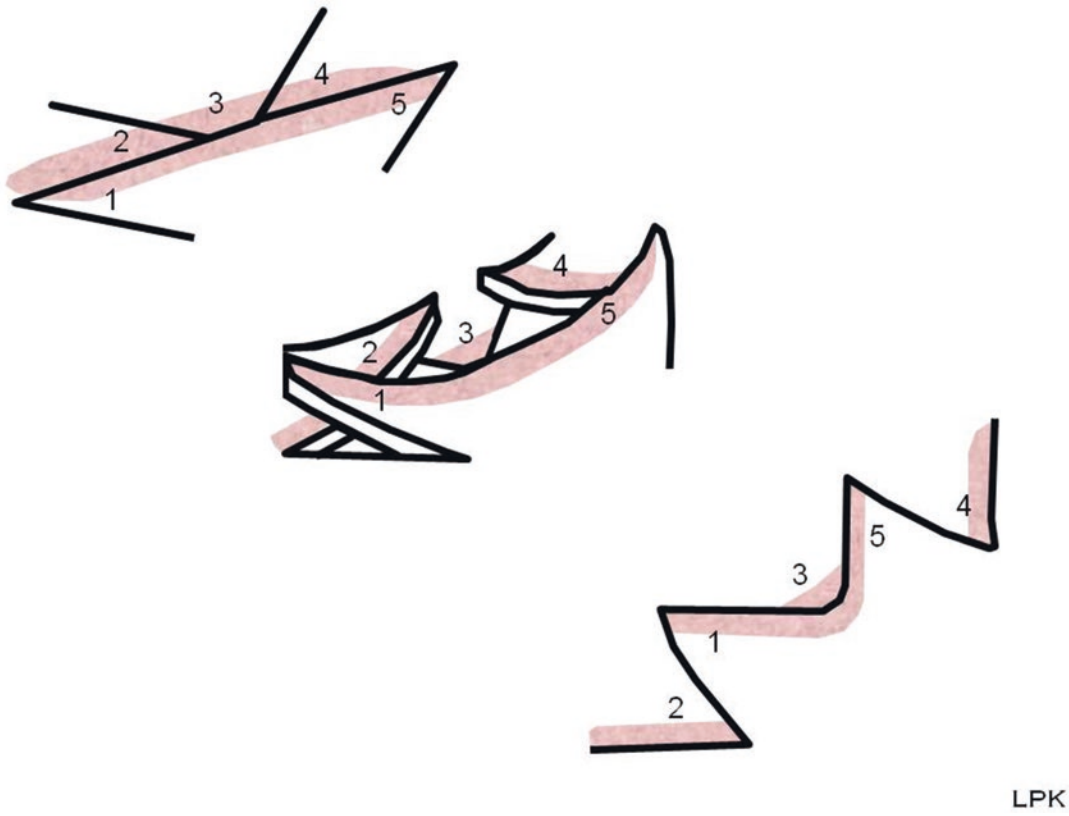

Fig. 6 Double opposing Z-plasty (scar: pink)

6.5 Regional and Distant Flaps

When the defect is not immediately adjacent or far from the defect, regional flaps and distant flaps are good options for reconstruction.

Regional flaps include an intact vascular pedicle which is connected to the soft tissue that is supposed to be transferred to another location. The soft tissue can be moved over or under healthy tissue to the defect/recipient site. A commonly used example for regional flaps is the pectoralis major flap.

A distant flap involves a donor site, which is far from the defect. The mode of transfer might be direct or microvascular. Direct flaps, such as the forehead flap or the groin flap involve direct approximation of the recipient bed to the donor site. These flaps require a second operation to divide the pedicle.

6.5.1 Free Tissue Transfer

The evolution of microsurgery and free tissue transfer has dramatically expanded the functional and aesthetic potential of reconstructive surgery. Due to microvascular anastomoses, free transfer of single or compound tissues and replantation of amputated parts are possible. Moreover, by using a free tissue transfer single-step reconstructions are principally possible. For free flaps, the vessels must be disconnected for the transfer. After preparation of the recipient site and its vessels, the artery and vein of the flap are reconnected microsurgically to the recipient site vessels.

6.5.2 Perforator Flaps

Based on the septocutaneous perforator vessels, the perforator flap was developed. Thus, Song and co-workers described in 1984 that the lateral femur region can serve not only as a skin harvest

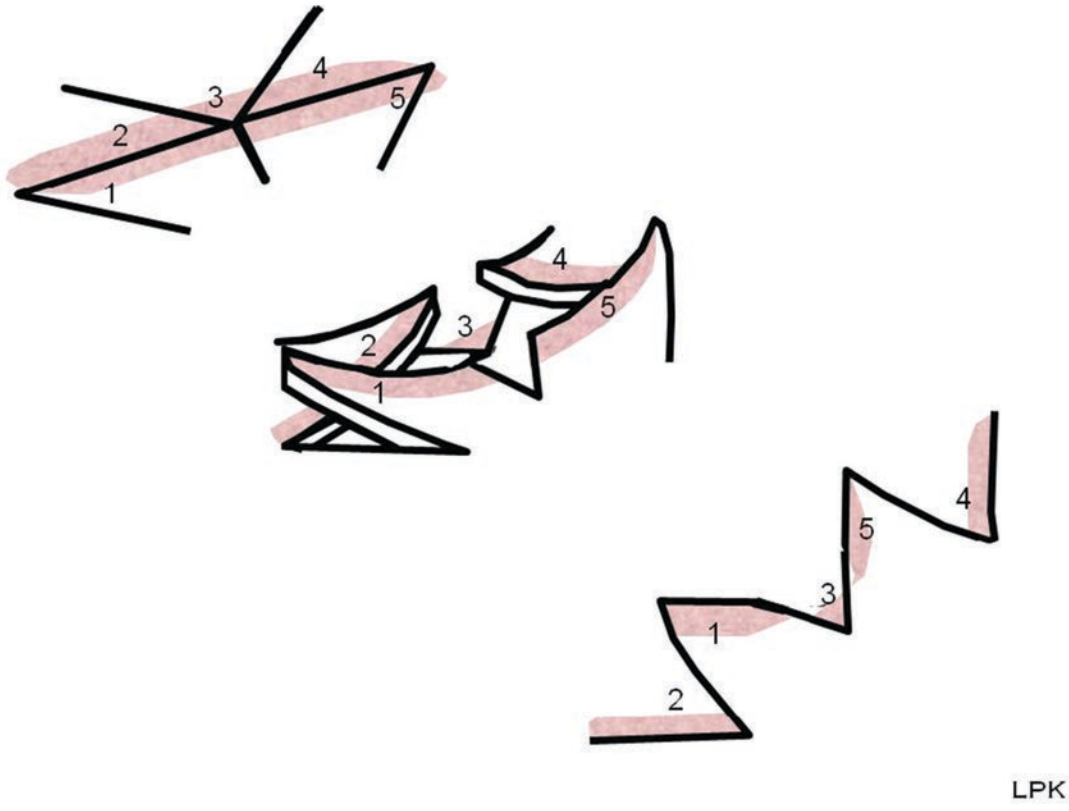

Fig. 7 Modified double opposing Z-plasty (scar: pink)

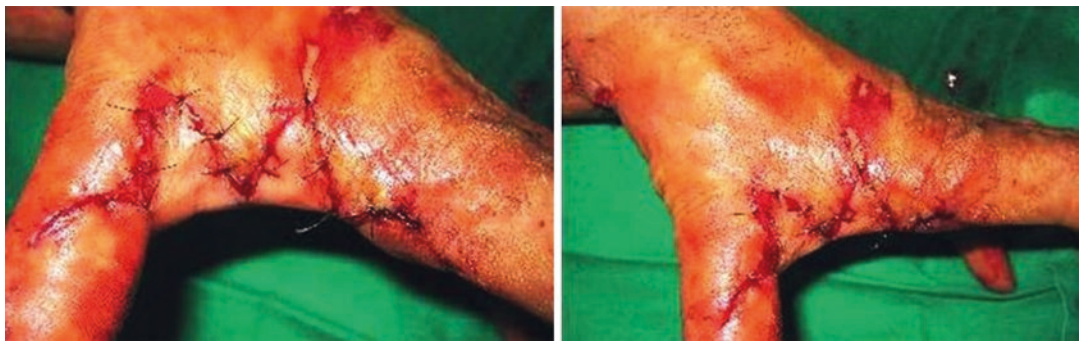

Fig. 8 Scar correction by use of a modified double opposing Z-plasty (1. Web space)

place, but also as the donor side for the "antero lateral thigh (ALT)" flap based on a long pedicle (see Figs. 12 and 13) [23]. Then, Koshima and colleagues from Japan refined exemplarily the ALT-transfer subsequently. In 1989, Koshima introduced an abdominal skin and fat flap based on the inferior epigastric vessels and muscle perforators. Since the publication of Saint-Cyr et al., the perforasome/angiosome theory has gained more relevance in vascularized free tissue transfer. A perforasome is defined as a specific territory perfused by a single perforator branch. Thus, every clinically significant perforator can become either a free or a pedicled perforator flap [24, 25].

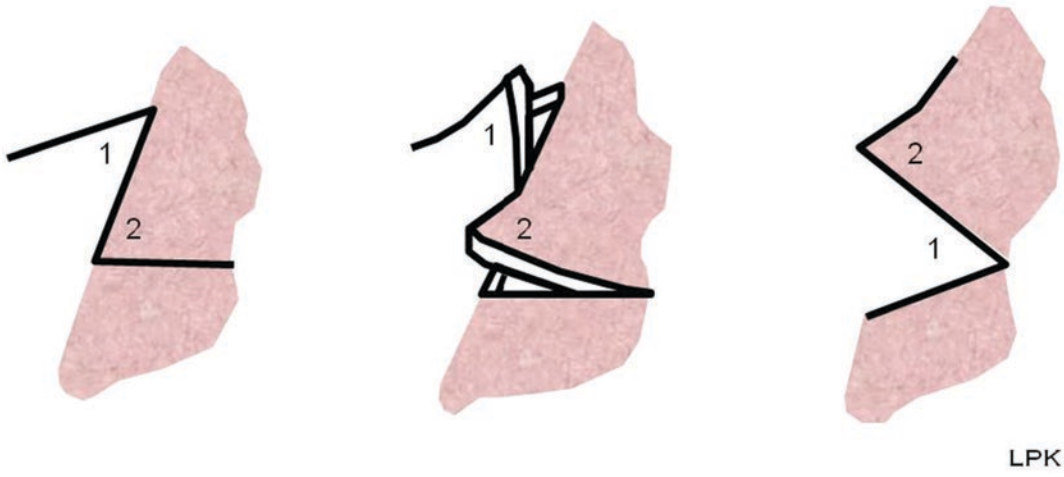

Fig. 9 ¾ Z-plasty or half-Z (scar: pink)

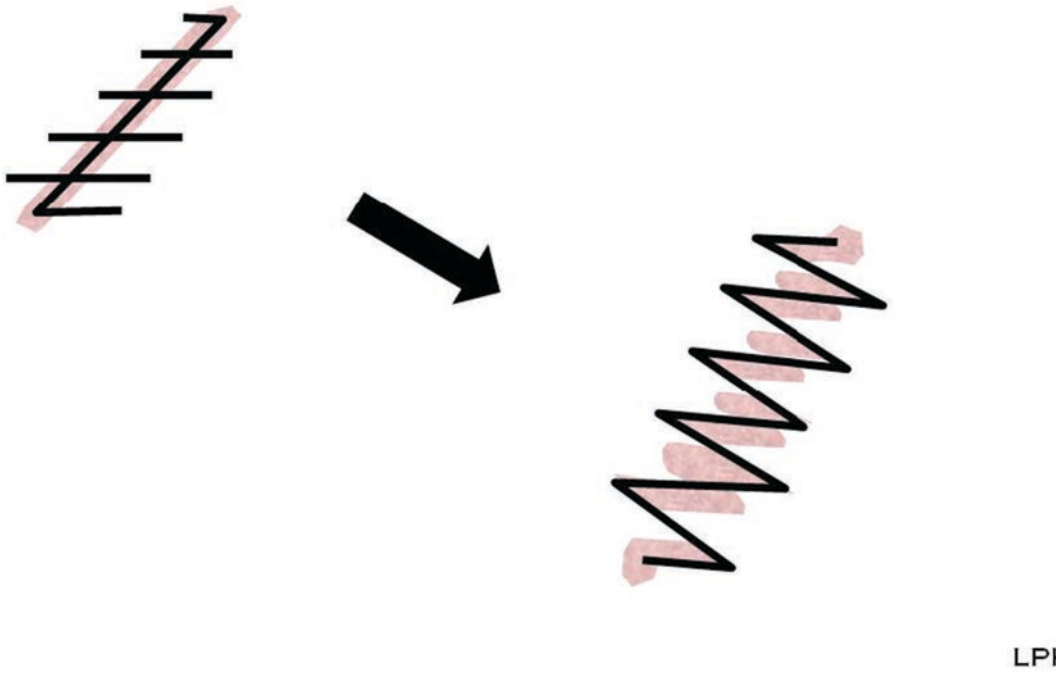

Fig. 10 Multiple Z-plasties (scar: pink)

7 Composition of Flaps

The described local, regional, and distant flaps can contain a variety of tissues. Thus, it is possible to categorize them in [26]:

- Skin
- Muscle
- Musculocutaneous
- Fasciocutaneous
- Osteocutaneous

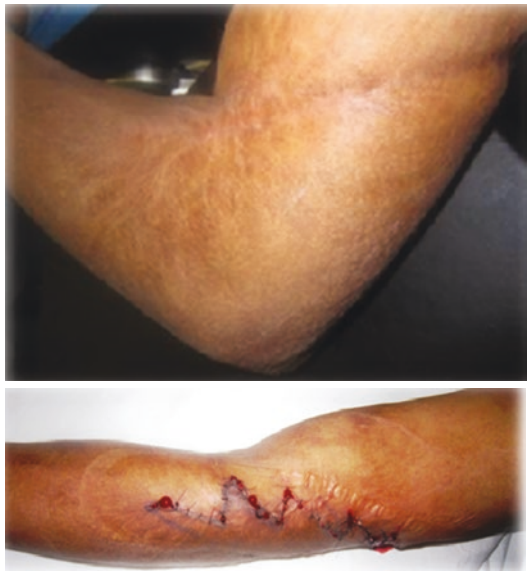

Fig. 11 Scar corrections by use of multiple Z-plasties (elbow)

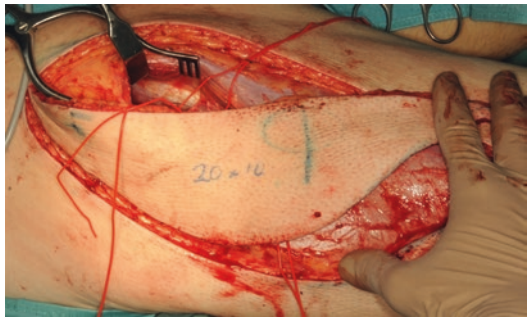

Fig. 12 ALT flap harvesting

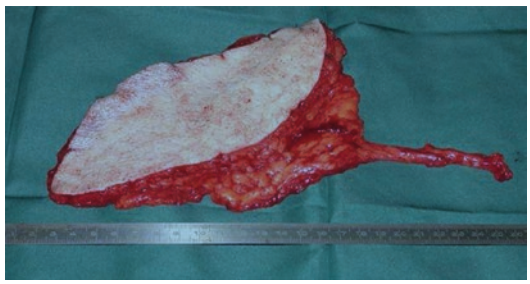

Fig. 13 ALT flap after harvesting with a long vascular pedicle

7.1 Skin

These flaps are mostly used as local flaps like the random pattern flap (e.g., Z-plasty-flap). The random pattern flap has no specific blood supply. Thus, these flaps have to adhere to some rules regarding size and shape (i.e., ratio of base and length of the flap). These flaps are suprafascial flaps which contain skin and subcutaneous tissue.

7.2 Muscle

Muscle flaps have a very good vascularization. If the overlaying tissue is not transplanted too, the flap can be covered with split-thickness grafts. These flaps can be used not only for covering defects but also for functional purposes (e.g., elbow flexion with a pedicled latissimus flap or facial reactivation with a temporalis transfer).

7.3 Musculocutaneous

Inclusion of not only the skin but also the subcutaneous tissues and the fascia and the muscle is necessary to fabricate a skin flap to reconstruct a tissue defect in individuals with deep burn injuries. That is, fabricating a flap in a burned area is possible if the underlying muscle or the fascia is included in the design [27].

7.4 Fasciocutaneous

Fasciocutaneous flaps usually contain skin, subcutaneous tissue, and fascia including the circulation of prefascial and subfascial plexus. These flaps can also be raised without skin as fascial flaps.

7.5 Osteocutaneous

In order to replace bones defects on, e.g., extremities and head, it is possible to raise flaps contain-

ing a vascularized bone with a defined blood supply. Osteocutaneous flaps can contain skin, subcutaneous tissue, or fascia too.

With the advent of microsurgical techniques, transplanting a composite tissue can be carried out with minimal morbidities. The regimen, in caring for burn victims, however, may be limited because of a paucity of donor materials. It is ironic that burn patients with suitable donor sites seldom require such an elaborate treatment, but those, who need microsurgical tissue transplantation, are inevitably without appropriate donor sites because of extensive tissue destruction.

7.6 Composite Tissue Allotransplantation

Composite tissue allotransplantation (CTA) of parts of the face, or forearms and upper extremities is a young area of transplantation medicine [28–31]. The first clinical results are promising in comparison to the first reports of the organ transplantation although the medium-term and long-term problems, for example, tumor induction by the immunosuppression as well as the chronic rejection must be considered. This is not an unimportant fact because CTA are normally not of vital importance [32]. Nevertheless, for the affected persons, who must live in social isolation with exhausted reconstructive measures or prostheses, such operations may result in a dramatic improvement concerning quality of life. However, it is important to mention that currently only a high selected small number of highly motivated patients are candidates for a CTA.

7.7 Regeneration: Tissue Engineering

Tissue regeneration and Tissue Engineering has gained relevance for reconstructive surgery [33–36]. Czerny transplanted in 1895 a lipoma for mamma reconstruction and fat injection was described among other things by Eugene Holländer in 1910 within a patient with "progressive decrease of the fatty tissue." Erich Lexer dedicated in the first part of his book free fat transfers nearly 300 sides. In 2001, it was demonstrated that beside fat cells also "adipose-derived stem cells" (ADSC) other cell populations in the fatty tissue are usable for these purposes. The transplantation of ADSC was able to regenerate full-layered cartilage defects in the animal model [37]. The stem cell-associated fat cell transplantation in patients with a radioderm has led to improved healing. Moreover, fat cell transplantation is not only able to improve volume and contour defects, but also skin quality [38–40]. However, ADSC and other stem cells seem to have a promising effect on wound healing after burn injuries. Several studies have shown this although mostly in animals [41]. The application in human is still at its beginnings and more studies are needed to integrate stem cell treatments for burn patient in daily clinical routine.

7.8 Robotics/Prosthesis

As a last resort, when all reconstructive measures fail, myoelectric prostheses seem to be very promising. These have improved significantly during the last and current decade by introducing targeted muscle transfers (TMR) to the armamentarium of reconstructive surgery [42–44]. Modern myoelectric prostheses have multiple degrees of freedom that mandate a complex control system to provide dependable use for the patient. A recent study has also shown a new approach for myoelectric control by decoding the motor unit activity of the muscles [45]. However, targeted muscle reinnervation together with the provision of a myoelectric prosthesis with several degrees of freedom an approach and can be a solid alternative if all other reconstructive attempts fail. Bionic solutions in medicine are advancing and can offer solutions and possibilities that have been unthinkable only a few years ago.

8 Summary

During the last decades, procedures and regimen of burn treatment have changed. The survival rate has improved due to a regimen with early debridement and wound coverage. In the initial phase with a biological dressing and later with autologous skin grafts. On the one hand, the improvement of survival rates is a pleasant development; on the other hand, it caused an increased demand of reconstructive surgeries on burn patients.

Unsightly hypertrophic scar, scar contracture, affecting particularly the joint structures, and missing bodily parts are still the most common sequela of burn injuries today.

The difficulty concerning burn reconstruction is largely due to a lack of adequate donor sides, but due to the improvements in reconstructive surgery better results are achievable. Newer areas like "composite tissue allotransplantation" of compound tissues like arms or parts of the face, the prosthesis and the regenerative medicine with "tissue engineering" have already entered the clinical routine and will be able improve the results obtained by burn reconstruction.

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