Surgery - Procedures, Complications, and Results

BURNS

PREVENTION, CAUSES AND TREATMENT

Emily S. McLaughlin
Ava O. Paterson
Editors

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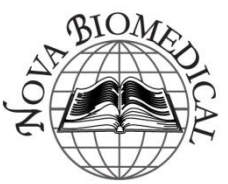

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CONTENTS

PREFACE

This book presents topical research in the study of the prevention, causes and treatment of burns. Topics discussed in this compilation include emergency burn care; nanotechnology and nanomedicine advancements in burn therapy; post-burn hand deformities; the role of apoptosis in burn injury; burns during arthroscopy due to the use of electrosurgical devices; the body's local and consecutive, systemic pathophysiological reaction to thermal lesions; the burn reconstructive units on the face and neck; use of modern day technology for pain management during burn injury rehabilitation; carbon monoxide intoxication in burns; the clinical application of Versajet Hydrosurgery System in burn debridement and escharotomy techniques in burn injuries.

Chapter 1- Burn injury is damage to the skin or other body parts caused by extreme heat, flame, or contact with heated objects or chemicals. The World Health Organization estimated that 322000 people die each year from fire related burns with >95% of these occurred in developing countries. In UK, it accounted for 175000 emergency department attendances and 15000 admissions. A further 250000 patient were managed in the community by general practitioners and allied professionals. A survey in 1998 showed that up to 58% of UK ambulance services had no specific treatment policy for burn patients. In Ireland and Australia, only 23% and 39% respectively, had employed the correct first aid burn management in studies conducted on their primary carers. Early burn management, from the moment of contact to eventual hospital arrival, are important to reduce the potential morbidity and mortality of burn victims. The initial management of burn from removal of patients from zone of incident to the topical administration of cool water has been shown to significantly reduce the extent of injury of burn patients. Further critical and timely assessment and management of these patients, pre-hospital and on arrival to emergency department, improve their chances of survival through adequate airway management and resuscitation. The need for emergency surgical procedure from emergency department to operating theatre should also be instituted when warranted without delay. Here, we review the pathophysiological rationale and evidence of practice behind each of these steps, from the first aid burn treatment to their assessment and resuscitation, and finally emergency procedure, together with their ancillary treatment, in practice.

Chapter 2- Successful burn therapy remains to be a challenge in respect to its remaining scaring and functional and cosmetic outcome. The enhancement of dermal and epidermal regeneration is the ultimate aim in burn treatment. Recently, several promising lines for improved burn therapy have been proposed, with the focus of this review being on

nanotechnology and nanomedicine-based systems. An ideal system should achieve permanent skin regeneration within both dermal and epidermal tissues, and provide good functional and aesthetic characteristics. Topical formulations destined for administration onto the skin need to posses optimal mechanical properties (such as spreadability), bioadhesion, acceptable viscosity and controllable release of active ingredients. The review discusses the current status, potentials and limitations for several of most promising research lines within the area of nanotechnology and nanomedicine. In addition, the use of *in vitro* and *in vivo* models as evaluation tools for nanomedicine destined for burn therapy is discussed.

Chapter 3- Optimal hand function is a crucial component of a high-quality survival after burn injury. This can be achieved only with a coordinated approach to the injuries.

Aim - To evaluate the clinical and functional outcomes of patients with burn's hand injury.

Methods - A retrospective review was carried out of the case notes of the patients. The case notes included the clinicians' notes and the nurses' entries during admissions in the Burns Unit at Selly Oak Hospital, University Hospital of Birmingham NHS Trust, outpatients clinics and correspondence with General Practitioners (Family Physicians).

Results - A total number of 22 patients were evaluated. 16 patients were children and 6 adults. The mean percentage of body surface burned was 10, 8 %. The most common type of burn was scalds. The mean interval between burn injuries and first release was 5, 3 years. Z-plasty was used in 8 cases, FTSG in 7, STSG in 12, W- plasty in 8. The ROM was full in 10 hands, good in 10 and fair in 3.

Conclusion - The findings suggest that with a multi-disciplinary team approach, proficient with the concepts and execution of appropriate treatment protocols, consistent results achieving maximum potential can be obtained for a patient with a burned upper limb.

Chapter 4- Apoptosis is a significant mode of cell death following reperfusion injury in burn wounds. The zone of stasis in partial thickness burn wounds is exposed to oxidative stress resulting from ischemia-reperfusion injury. Nitric oxide (NO) plays a significant role in the initiation of the inflammatory cascade following ischemia and oxidative stress during the reperfusion period. Recent results suggest that i-NOS inhibition in partial thickness burn wounds reduces apoptotic tissue injury in the zone of stasis. This therapeutic intervention may have clinical application for tissue preservation in the thermally injured patients. In this chapter we also give a comprehensive overview about the current knowledge and the key role of apoptosis in research innovations in the field of burn injury. Burn injury is a complex traumatic event with various local and systemic effects, apoptosis is affecting several organ systems beyond the skin. Recent advances in the comprehension of mechanisms underlying systemic complications of thermal injuries have contributed to uncover part of the cellular and molecular basis that underlie such changes. Recently, apoptosis has been considered playing an important role in the development of such pathological events.

Chapter 5- There were thousands of arthroscopic procedures performed in the United States each year. Roughly 85% of all surgical procedures will employ some type of electrocautery. Burns and other thermal injuries, from direct electrocautery and arthroscopic devices, can create lifelong morbidity and even mortality.

The components of electrocautery are the power generator, a handheld monopolar or bipolar electrode, and, if necessary, a patient return electrode. Heat generation is dependent upon several factors, including type and duration of the current, type of tissue, tissue cross section, humidity of the skin, and more.

In monopolar electrocautery, the current, which has entered through a single, small-surface-area point, must be dissipated and complete the circuit through a patient return electrode (PRE). The current, which entered the body though the small surface area electrode, exits through a large surface area pad. Safety guidelines regarding skin temperature are built into some electrocautery devices.

"Aberrant grounding" can occur with a wide variety of operating room materials as well. These are unexpected areas of low or high resistance which influence the direction of current and can be a risk factor for burns.

Chapter 6- This chapter provides an overview of the body's local and consecutive, systemic pathophysiological reaction to a thermal lesion. In addition to immunological processes at the cellular level, the development of systemic inflammatory response syndrome (SIRS) is also explained within the scope of the pathophysiological reaction to the burn injury. Building on this, the two current theories (the "two-hit model" and the model of posttraumatic immunosuppression) on how multiple organ failure develops will also be discussed. The resulting pathophysiological responses to the burn trauma by the individual vital organs will be explained. In addition, this chapter will also discuss the options presently available to treat organ failure.

Chapter 7- The concept of aesthetic units and subunits has not always been considered in functional reconstruction of the face and neck in extensively burned patients, since prevention of scar contracture and functional reconstruction are foremost considerations. Here, we review previous works in this field and revisit the concept of "aesthetic units" and "aesthetic subunits". We advocate the novel concept of "burn reconstructive units," which have been categorized into ten units: 1. forehead unit, 2. nasal unit, 3. eyelid unit, 4. cheek unit, 5. upper lip unit, 6. lower lip unit, 7. mental unit, 8. auricular unit, 9. nape unit, and 10. anterior neck unit. "Burn reconstructive units" are designed to prevent and release scar contracture in addition to improving the aesthetics of the wound, and are thus considered as "functional units" in contrast to "aesthetic units." It is considered that burn reconstructive surgeons must strive to achieve both functional and aesthetic reconstruction, and should consider various options on a case by case basis.

Chapter 8- With advances in medicine bringing about significant improvements in critical burn care management; the chances of surviving even the most extensive burn injury are high. Needless to say, individuals who sustain extensive burn injuries and indeed survive are often left with severe physical disabilities and require comprehensive burn care management and rehabilitation for longer periods of time. Burn rehabilitation is primarily aimed at reducing the development of physical complications and minimizing functional disability; ensuring prompt societal re-integration and optimal quality of life post-injury. Rehabilitation therefore remains, and will probably always be, an indispensable component of burn care management programs.

Chapter 9- Carbon monoxide (CO) intoxications are frequent and can lead to high morbidity and mortality, involving multiple organ systems (e.g. lung, heart, peripheral and central nervous system) and undetected CO exposure can be fatal. It is a toxic, colorless, odorless, tasteless, and non-irritating gas. From the available data, carbon monoxide poisoning is the most common cause of injury and death due to poisoning worldwide. Prevention remains a vital public health issue, requiring public education on the safe operation of appliances, heaters, fireplaces, and internal-combustion engines, as well as increased emphasis on the installation of carbon monoxide detectors. In Burns, CO

intoxication CO binds hemoglobin 230-270 times more avidly than oxygen, so even small concentrations can result in significant levels of carboxyhemoglobin (COHb). The clinical picture is untypical and in many times is not related to the amount of COHb. In severe cases, CO intoxication can lead to coma or even death. In case of pregnancy, Carbon monoxide also crosses the placenta and combines with fetal hemoglobin, causing more direct fetal tissue hypoxia. Additionally, fetal hemoglobin (Hbf) has a 10 to 15% higher affinity for carbon monoxide than adult hemoglobin (HbA), causing more severe poisoning in the fetus than in the adult. Arterial blood gas (ABG) is one of the most reliable Investigations to detect the level of COHb but the main disadvantage of ABG with COHb testing is the unavailability in pre-hospital rescue conditions. To date, COHb is routinely used as a marker for detecting CO intoxication. It is suggested that the lactate level may be a useful prognostic factor, but this is still controversially discussed. As a basic role in the treatment, an immediate supply of high dose oxygen is essential to reduce mortality and long-term morbidity. Furthermore, hyperbaric oxygen therapy (HBO) is now standardized in many centers worldwide. Increased elimination of COHb clearly occurs but on the other hand, the benefit of HBO treatment is still under current debate. Treatment of CO intoxication could be very challenging especially those cases associated with Burns. Thus multidisciplinary approach should always be considered involving Burn surgeons, Emergency Room (ER) physicians, Otolaryngologists, Internists and Anesthesiologists.

Chapter 10- Burns depth assessment in the early stage of burn injury is a crucial point in determining the need for an early surgical intervention. It is very important to accurately assess the burns depth as early as possible and decide whether these are superficial and will heal spontaneously or deeper and warrant earlier excision and grafting. Traditionally, visual and tactile assessment is an easy, fast and non-invasive method. Such method is considered to be subjective and sometimes inaccurate. The ideal method should be non-invasive, cheap and easy to use, have minimal risks and side effects and most importantly to reliably predict healing chance and time with estimation of scar risk formation. This assignment will examine the effectiveness of the Laser Doppler Image (LDI) in assessing burns depth in the early stages after the injury. This will be through literature search of related studies as well as assessing this tool's potentials using the concept of clinimetrics. It is a methodological discipline concentrating on clinical measurement quality. It is essential to examine a new instrument's clinimetrics properties before applying it in clinical practice. The LDI as a tool for burns depth assessment seems to show high validity, reliability, reproducibility, responsiveness and acceptability, further prospective studies are important to re-assess this tool and its clinimetrics. A clear understanding of the limitations of LDI is needed to put the current research in perspective to find the right clinical application for LDI

Chapter 11- The primary goal of acute burn management is debridement of necrotic skin and underlying tissue to expedite healing. Early debridement (within 2-3 weeks) is superior to late debridement for deeper burns that are unlikely to heal spontaneously. Heimbach (1987) suggested two types of burn excision. Tangential (sequential) excision removes nonviable sparing viable tissue, with an end point of punctuates bleeding judged by the surgeon. Excision down to fascia is used in large full-thickness burns when patient's mortality is the main concern against bleeding and long operative time.

The choice of the debridement method depends on many factors including burn depth, amount of slough, patient's condition and surgeon's experience. Jeffery (2007) suggested disadvantages of different methods. A guarded blade, such as Watson knife, remains an issue

of depth perception and difficult to correctly apply to different body parts causing unnecessary debridement of healthy tissue and increased blood loss. Also, the ‘’shelving’’ effect due to variances in excision slopes conflict with the uniform surface needed for reconstruction and the ‘’stuck on’’ appearance due to excessive tissue at the periphery of the debrided area. Dermabrasion debridement using dermatomes and rotating burr or dermabrader allow more precise debridement reducing healthy tissue loss, but can be difficult to use due to increased bleeding. Ablative laser, such as CO2 laser, is rarely used because of practical limitations and it also leaves a thermally damaged layer (0.1 mm thick) on the surface.

Chapter 12- The initial treatment of burns is in most cases, performed by health care personnel not specialized or experienced in treating burns. In circumstances where rapid transportation to a burns center is not possible, such as in hostile environments but also in Western Europe and North America, there can be a vital indication to perform escharotomy during the first period of treatment at a primary hospital. The indications for escharotomy of the neck, upper and lower extremities, and the thoracic and abdominal wall are discussed. The proper operative technique and post-surgical treatment of these procedures are described.

Chapter 13- Burns are important causes of emergency care for children and adults around the world. Most burn accidents occur at home and male persons are the most affected victims. The main cause of burns in children are hot fluids and, in adults, fire. A burn is a skin tissue injury and can be classified, according to the agent, as physical, chemical, electric and radiant and, according to the injury characteristics, considering the depth (superficial, partial thickness and full thickness burn) and extent of the burned body surface. The following factors influence burn prognoses: depth and extent of the injury; causal agent; contact time between skin and causal agent; age, injury by inhalation and airway burns; preexisting diseases; associated traumas and infection. Like for the burn prognosis, some factors influence burn victims’ rehabilitation process and can be directly related to quality of life. It is known that adaptation after the burn implies a long process, influenced by changes in body structure and functioning, body image, emotional condition and socioeconomic and cultural context the person is inserted in. This chapter presents the result of an integrative literature review on impact of burns on the health-related quality of life of burned patients in the rehabilitation phase. Four independent reviewers used six electronic databases (LILACS, PubMed, PsycINFO, CINAHL, Scopus and ISI Web of Science) for the search, based on previously defined inclusion and exclusion criteria. The analysis of 32 studies revealed that burns patients’ health-related quality of life is associated with physical, emotional and social aspects. In general, the studies showed that greater trauma severity, inadequate coping mechanisms, dissatisfaction with one’s body image, difficulties to establish interpersonal relations and the presence of post trauma distress are associated with a worse health-related quality of life. Return to work and longer time after the trauma are predictors of a better health-related quality of life. In the rehabilitation process, victims’ individual and social aspects should be taken into account, aiming for their reinsertion in society with as little influence as possible from the trauma and with a better quality of life.

Chapter 14- After an epidemiological analysis of psychiatric disorders as a consequence of burns and also psychiatric aspects of burn victims before the accident, this paper discusses the correlation between psychiatric disorders and burns from the epidemiological, etiopathogenetic and clinical-therapeutic aspects.

Burn patients often suffer from psychiatric disorders and there is a clear connection between the extent and/or severity of injuries (TBSA) and mental illness, particularly anxiety, mood disorders, and post-traumatic stress disorder.

The occurrence of psychiatric disorders (mainly substance or alcohol abuse/dependence, suicidal behaviour, schizophrenia and personality disorders – antisocial or borderline) is a clear-cut risk factor for those with burn injuries.

The occurrence or onset of psychiatric illness during burn hospitalization or recovery is a negative factor for wellbeing and also for the quality of life in the medium-long term.

A burn injury is a traumatic experience for patients, not only as regards psychological aspects (no integration of the traumatic experience with self-perception of life) but also personal ones (knowledge of self-vulnerability, difficulty in accepting the new aspect of the body, with its possible deformation and scars) after trauma. All aspects which may refer to primordial and psychoanalytic fear of death must be taken into consideration. It is also necessary to consider the concepts of accident proneness and consequent pre-burn impulsivity, which may anticipate/represent a person's predisposition to a traumatic event.

All these concepts have clinical and therapeutic importance for multidisciplinary care.
This chapter focuses on the relationship between burn injuries and psychiatric illness: post-traumatic stress disorder (acute and chronic), affective disorders, and personality traits. They must all be examined not only as regards their outcomes but also the patient's pre-trauma psychopathology and susceptibility. Also of importance is facing therapy for all these disorders and its correlation with burn care (in terms of length of hospital stay, quality of life, and functional and psychological results).

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Chapter 1

EMERGENCY BURN CARE IN PRACTICE: FROM FIRST CONTACT TO OPERATING THEATRE

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ABSTRACT

Burn injury is damage to the skin or other body parts caused by extreme heat, flame, or contact with heated objects or chemicals. The World Health Organization estimated that 322000 people die each year from fire related burns with >95% of these occurred in developing countries. In UK, it accounted for 175000 emergency department attendances and 15000 admissions. A further 250000 patient were managed in the community by general practitioners and allied professionals. A survey in 1998 showed that up to 58% of UK ambulance services had no specific treatment policy for burn patients. In Ireland and Australia, only 23% and 39% respectively, had employed the correct first aid burn management in studies conducted on their primary carers. Early burn management, from the moment of contact to eventual hospital arrival, are important to reduce the potential morbidity and mortality of burn victims. The initial management of burn from removal of patients from zone of incident to the topical administration of cool water has been shown to significantly reduce the extent of injury of burn patients. Further critical and timely assessment and management of these patients, pre-hospital and on arrival to emergency department, improve their chances of survival through adequate airway management and resuscitation. The need for emergency surgical procedure from emergency department to operating theatre should also be instituted when warranted without delay. Here, we review the pathophysiological rationale and evidence of practice behind each of these steps, from the first aid burn treatment to their assessment and resuscitation, and finally emergency procedure, together with their ancillary treatment, in practice.

1. INTRODUCTION

Burn injury is damage to the skin or other body parts caused by extreme heat, flame, or contact with heated objects or chemicals. The World Health Organization estimated that 322000 people die each year from fire related burns with >95% of these occurred in developing countries. [1] The mortality rates were much greater at both ends of the age spectrum. Thirty-eight percent of all burn deaths were due to multiple organ failure and only 4.1% were due to burn wound sepsis. [2] The biggest factor in burn mortality was inhalation injury with increased mortality to 26.3% in the 6.5% of burn patients admitted with inhalation injury. [2]

In UK, burns accounted for 175000 emergency department attendances and 13000 admissions, and a further 250000 patient were managed in the community by general practitioners and allied professionals. [3] Although recent data from Burn Repository in USA showed significant improvement of overall burns mortality, there are still many areas that can be improved especially in the early stage of burns treatment to optimize chances of survival and outcome. [2] A survey in 1998 showed that up to 58% of UK ambulance services had no specific treatment policy for burn patients. [4] In Ireland and Australia, only 23% and 39% respectively, had employed the correct first aid burn management in studies conducted on their primary carers. [5, 6] Equally, a review of the management of minor burns within the emergency departments of hospitals in Ontario, Canada, showed that 70% of responding physicians would not measure the extent of the burn area when making an assessment, whereas 45% failed to discuss analgesic requirements. [7] Based on these data, there is still much room to improve in the basic care of burn victims.

2. PATHOPHYSIOLOGY OF BURNS

Burn from thermal source inflicts damage through various mechanisms, both locally and systemically, through direct injury and reactive physiology. The natural functions of skin are to act as a barrier to bacteria and prevention of water loss through its epidermal layer. The deeper, dermal layer provides mechanical strength and integrity through its abundant connective tissue composition, and nourishment to epidermal and dermal layers through myriad of vascular plexuses. The dermal layer is also the home to many dermal appendages such as sweat glands and hair follicles, which houses regenerative epidermal cells that are capable of replenishing injured skin. When such functions of skin are compromised, attending physician should institute treatments that will minimize the injury and compensate its deficits through adequate first aid and resuscitation. Early burns management, from the moment of contact to eventual hospital arrival, is one of the most important determinant factor in reducing the potential morbidity and mortality of burn victims. In USA, approximately 75% of severe burn deaths occur at the scene of the accident or during initial transport. [8]

The pathophysiology of thermal burn injury is related to the initial distribution of heat within the skin with its severity dependent upon the temperature of the source of insult and the duration of contact. [9] On a cellular level, the initial response to thermal injury involves direct heat-induced protein denaturation and cell death. This is followed by inflammation and ischemia-induced injury, which resulted in burn of varying skin depth. Because skin is a good

insulator, most burns generally involve only the epidermis or part of the dermis. Only with prolonged exposure do burn encompasses the entire dermis or extend beneath the dermis into subcutaneous tissue such as fat, muscle, and bone. However, similar extent of burn can also occur with short exposure to an object of high temperature. For instance, a thermal blistering injury can occur after 5 minutes of exposure to water at 48.9°C (120°F) or after just 1 second of exposure to water at 68°C (155°F).

The depth of burn is a dynamic process, as popularly described by Jackson. [10] The histopathology of burn consists of three concentric zones with the zone of coagulation being the area closest to the heat source. The tissue in this zone either is entirely necrotic or undergoes severe denaturation of proteins and forms an eschar. This is a zone of irreversible injury. Just below the zone of coagulation is a zone of stasis, where there is only modest denaturation of macromolecules but characterized by hypoperfusion of tissue due to significant edema and stasis. This has been attributed to capillary leak and cell membrane disruption in this zone. Beneath the zone of stasis is an area of hyperemia, where blood flow gradually increases, becoming particularly prominent by about 7 days after the injury. [11] Although tissue in the zones of stasis and hyperemia are at risk for necrosis, they are potentially salvageable given optimal intervention that preserves perfusion of these zones. [10] Conversely, a burn that appears superficial may become deeper over a period of 48 to 72 hours, with the zone of stasis becoming necrotic in the face of suboptimal treatment. [12] This is especially likely to happen if the wound becomes infected or there is poor perfusion of the affected area. Adequate fluid resuscitation is essential to maintain tissue perfusion in this dynamic zone. [13 14]

Although the mechanism of primary tissue loss in burn occurs as a result of local protein denaturation and tissue necrosis, this process is rapidly followed by activation of toxic inflammatory mediators, especially in the perfused subsurface. [12] The release of vasoactive mediators translates local edema into both local and systemic fluid shifts that exacerbate hypoperfusion in vulnerable tissue, specifically in the zones of stasis and hyperemia. [12, 15] Oxidants and proteases further damage skin and capillary endothelial cells, potentiating ischemic tissue necrosis. [12, 15] When the burn exceeds 20% of the patient's body surface, the local tissue response becomes systemic with potential hazardous effect on distant tissues and organs. [16-18] Sequelae such as edema and altered perfusion promote progression of injury beyond the degree of initial necrotic area through worsening fluid regulation and systemic inflammatory responses. [12, 15] Activation of complement and coagulation systems causes thrombosis and release of histamine and bradykinin, leading to an increase in capillary leak and interstitial edema in distant organs and soft tissue. [16] Secondary interstitial edema and organ dysfunction from bacterial overgrowth within the eschar can then result in systemic infection. Activation of the proinflammatory cascade and the counter-regulatory anti-inflammatory reaction then lead to immune dysfunction. [16] This increases the burn patient's susceptibility to sepsis and multiple organ failure. The systemic response to burn also leads to a hypermetabolic state, doubling normal physiologic cardiac output over the first 48 h post-burn. [19] This is mediated by hugely increased level of catecholamines, prostaglandins, glucagons, and glucocorticoids, resulting in skeletal muscle catabolism, immune deficiency, lipolysis, reduced bone mineralization, and reduced linear growth. These systemic metabolic changes in the burn patients may be present for a year after injury. Therefore, mitigating factors in early treatment to decrease these effects, which include adequate first aid and resuscitation, early excision of burn and grafting, control of sepsis,

supplemented nutrition through high-carbohydrate/high-protein diet, and the use of anabolic agents, need to be instituted as early as appropriate.

3. THE FIRST AID AND PRE-HOSPITAL CARE

All emergencies started onsite, at the site of initial incident. Emergency care should therefore, includes pre-hospital and en route care before actual arrival to emergency department. The first aid is emergency care or treatment given before regular medical aid can be obtained, and it serves to provide analgesia and halt the progression of burn. Walker et. al. summarized the consensus of the first aid management and pre-hospital care for burn victims to serve as a reminder for the carer as to the first priorities in caring for burn victims (Table A). [20]

Historically, first aid in burns treatment ranges from the use of natural to traditional or folk remedies over the centuries, to more recent recommendation from regulatory bodies based on clinical studies. The concept of 'first aid' was believed to be initially described by the Prussian surgeon (Surgeon General) Friedrich Von Esmarch (A.D. 1823–1908), with his work on 'Erste hilfe' first translated from German to English in 1882. [22] Modern first aid concept, as a set of trained drills and skills, dated only from the late nineteenth century. [23]

Table A. Consensus on first aid management of burn

SAFE approach	Shout or call for help Assess the scene for dangers to rescuer or victim Free or remove from danger Evaluate the casualty
Stop the burning process	Stop burning process by allowing patient to roll on the ground, use of blanket, water or fire extinguisher Remove clothing and accessories unless adherent to the patient Remove any jewelry, which may become constrictive Bring all clothing articles to the hospital for examination
Cooling the burn	Irrigate the burn area for up to 20 minutes with cool running tap water [21] Ice and very cold water should be avoided Place a cold wet towel over area of small burn (<5%) on top of polyvinylchloride film (e.g. Clingfilm) dressing Caution on hypothermia especially in children
Dressing the burn and victim	Polyvinylchloride film dressing to keep burn area clean and help in pain relief by covering the exposed nerve endings Use small sheet of dressings rather than large circumferential wrapping to avoid constricting effect Alternatively use water gel dressings to cool and dress [20] Wrap the patient in blankets or a duvet to keep warm

The use of cold water as first aid for burn has the greatest volume of supporting literature, compared to other therapies, and it has been a popular treatment throughout history. Early literature as far back as Galen (A.D. 129–199), Rhazes (A.D. 852–923), and Ibn Sina (980–1037) can be found to use cooled or cold water for burn. [24] In 1969, St John Ambulance first aid manual advocated irrigation of burn wound with cold water even though the duration of its application was never mentioned. [25] More recent studies by Rose among others indicated that treatment with cold water decreased pain and mortality by reducing damage to tissues. [26-33] However, conflicting reports continue to emerge on the benefit of using cooled water due to the lack of clear guidelines concerning the temperature of the coolant, time period of application and the effect of delay between a burn and the commencement of cooling. [34] Studies conducted by Cuttle et. al. have shown that the immediate use of 2-15^{o}C running, cold water for 20 min duration can increase healing by limiting the depth of burns, and promoted re-epithelialization over the first 2 weeks post-burn with decreased scarring at 6 weeks. [35, 36] This benefit was noticeable when treated for as little as 10 min duration, with maximum benefit observed at 3 h, and even when delayed for up to 30 min to 1 h. [34, 36]

Cold water reduces the extent of burn injury by cooling the tissue below the damaging temperature and subsequently assist burn healing by preventing cells from undergoing progressive necrosis 24–48 h after burn in the zone of stasis. [10, 26, 37] It causes a decrease in cell metabolism, which allow the compromised cells to survive a hypoxic wound environment, stabilize the vasculature by decreasing capillary leakage, increasing dermal perfusion and re-establishing blood flow, and dampens the inflammatory response to facilitate cell survival in the burn wound. However, because of the perceived potential for hypothermia after cold treatment, some researchers advocated treating burn wound with lukewarm or body temperature water. [38]

Warm water as first aid burn treatment was popular in the late 1800s to early 1900s. It was recommended that burned limbs should be soaked in body temperature water of 36.9 ^{o}C (98.4 ^{o}F) until suitable dressings could be found. [39-41] This was to decrease pain, and also prevent shock and infection. It was believed that the application of heat in smaller doses restores the tissue to normal. However, it was also recognized as early as 1899 that further heat application to burn simply causes more harm. [42]

On the other end of the spectrum, some early studies advocated direct use of ice and these were anecdotal at best. [32, 43] There were subjective observations that ice appeared to heal burn wounds with less damage and scarring. In 1799, Sir James Earle, who was a physician, reported good results with total immersion of burn wound in the coldest water possible or direct application of ice, sometimes for up to several days. [43] Over the years, various other ice immersion or application regimes have also been described, which conferred benefit in burn treatment. [44, 45] In the 1960s, Fay advocated cold air and ice pack treatment for large burns, stating that local refrigeration was bacteriostatic, provided pain relief and prevented surgical shock. [46] Modern first aid recommendations however, advise that ice deepens or worsens the injury. This was supported by Sawada et. al., who used a rat burn model, found that ice causes injury by causing prolonged vasoconstriction, which lead to ischemic necrosis. [47] Although Cuttle et. al. did not find ice treatment on burn to be damaging, their results were indifferent in comparison to untreated controls in porcine partial thickness burn. [35] The main risk associated with using ice for burn treatment is the risk of hypothermia. Any application of cooling treatments will increase the possibility of hypothermia especially in

children or patients with large body surface area burn as demonstrated in Ofeigsson's experiments. [26]

Other substances used for first aid burn treatment by native cultures are aloe vera and tea tree oil. Aloe vera has been shown to improve treatment of first and second degree burns in a clinical review by Maenthaisong et al. [48] It significantly shortens the wound healing time by modulating collagen response and inhibits the inflammatory process in the healing wound. [49-52] There are several hydrogel products on the first aid market based on tea tree oil such as Water-Jel®, Burnshield®, Burnaid® and Burnfree®. These products are recommended as first aid for burns, and have been adopted by Australian ambulance and paramedic services. They contain ≥90% water and melaleuca oil in a proprietary gel. To date, there is limited evidence that these products are beneficial for burn treatment, although they are reported to soothe the burn. [53, 54] Their effects were attributed to their anti-inflammatory, antibacterial and antifungal properties. [55-57]

Several other oils have also been recommended for first aid treatment of burn, namely lavender and thyme oil. [58, 59] There is some evidence that oils, especially those derived from plants, may act as antioxidants and either directly or indirectly scavenge oxygen-derived free radicals. [60, 61] One study has demonstrated that lavender oil possesses local anaesthetic, antibacterial, and antifungal properties, which makes it effective in healing wounds including burns. [58, 62] Thyme oil, from the herb thyme is used in Turkey as an excellent remedy for the treatment of burns and has been shown to also have antibacterial, antifungal and antioxidant properties. [59, 63] Other oils and creams used over the years to protect against excessive burn wound exposure to air were painted grease or butter, almond or cod-liver oil, olive oil, salad oil, castor oil or carron oil, linseed, lamp oil, or carbolic acid or thymol oil soaked cotton wool dressing, and Vaseline® or lanoline cream. [22, 39, 41, 64] Most other common household liquids have also been used as first aid to treat burn. There are reports in the literature of treatment with toothpaste, soy sauce, eggs, honey, ink, and traditional African wound treatments such as leaves, mud, burned snail shell, a mixture of urine and mud, and cow dung. [65-70] Many of these folk remedies are based on the idea that air should be excluded from a burn as quickly as possible.

4. ASSESSMENT AND REFERRAL

Most simple burns can be managed by general practitioners in primary care, but complex and major burns warrant a specialist and skilled multidisciplinary approach to optimize clinical outcome. Upon arrival to emergency department, the first decision to be made is whether a burn can be managed at the local facility or should be transferred to a designated burns center. Table B outlines the criteria for referral to specialized burns center. [71]

Other factors to consider include the presence of inhalational injury, adequate pain relief, home circumstances, nutritional requirement and continuity of care of the patient at home or in primary setting. If in doubt of the necessary meticulous burn care, the burn patient should be referred to burn center. Because burn wound evolves over several days, it should be re-evaluated within 3 to 5 days. [12, 72] Evaluation should confirm that the burn wound is progressing toward healing, and no risk of joint contracture or infection. Even small area burn that take more than 14 days to heal need to be referred to specialized center. [71] Although it

is possible to successfully treat the majority of partial thickness burns in the general hospital or community setting, full thickness burns should always be referred. [73] It is also advisable to refer to specialized burn center if the caring physician anticipates a potential need for physical or occupational therapy for their burn patient. Any failure to foresee such need is detrimental to the patient's recovery.

5. EARLY BURN MANAGEMENT IN HOSPITAL

Annually in the United Kingdom, around 175000 people attend emergency departments with burns from various causes. [3] Of patients referred to the hospital, some 16000 are admitted, and about 1000 patients need active fluid resuscitation. [71, 74] The number of burn related deaths average 300 a year. [71] All major burns should be managed initially according to the guidelines of the American College of Surgeons Committee on Trauma and the Advanced Trauma Life Support (ATLS) manual. [75-77] The survival data analysis from 1665 burns patients from the Massachusetts General Hospital identified three risk factors for death: age over 60 years, more than 40% of total body surface area burn, and inhalation injury. [78] Table C outlines the principles of emergency burn care as outlined in Emergency Management of Severe Burns (EMSB) course. [72, 75]

5.1. Assessment and Parallel Management of Immediately Life Threatening Injuries

Approximately 10 percent of all burns present with concomitant trauma. [79] These should be suspected, diagnosed, and managed following the guidelines of ATLS. [76] An important point to note is that in the emergency situation, attending surgeon should institute the steps in ATLS in parallel, often with the assistance of other medical personnel.

Table B. Criteria for referral to specialized burns center

If 10-40yo: ≥15% TBSA partial thickness burn or ≥5% TBSA full thickness burn
If <10yo or >40yo: ≥10% TBSA burns
Special area burns involving face, hands, feet and/or perineum, genitalia, joints
Circumferential burns
In extremes of age
Polytrauma
Significant co-morbid disorder
If surgical management indicated (deep partial thickness, full thickness burns)
Electrical burns

Table C. Emergency management of severe burns

Airway	Humidified O_2 at 8L/min (40%) ± Bronchodilators 100% supplement if suspecting CO poisoning (COHb ≥15% or altered level of consciousness suspicious of CO poisoning). If a patient has an isolated burn injury that is small and when no inhalation injury is suspected the oxygen may not be necessary ABG and other bloods (as indicated) Intubation as indicated
Burn assessment	Total body surface area (TBSA) Depth
Circulation and resuscitation	Parkland formula 4ml/kg/%TBSA burn (first half in the first 8 h from the time of incident and second half in the next 16 h) if large burn (≥15% TBSA adult, ≥10% TBSA child) Holliday-Segar formula for maintenance fluid (4ml/kg/h for the first 10kg, 2ml/kg/h for the second 10kg, 1ml/kg/h for subsequent kg of body weight) in children Two 16G IV cannulas but the cannulation itself should not unnecessarily delay the transfer time. This should be limited to two attempts only Ideally warm resuscitation fluid used Urinary catheterisation if ≥20% TBSA adult and ≥15% TBSA children. Urine output maintain ≥0.5ml/kg/h for adult, ≥1.0ml/kg/h if child >1 year old or <30kg, and ≥2.0ml/kg/h if <1 year old Reassessment every 15-30 min Fluid boluses of 5-10ml/kg in 15-20 min and/or increase the next hour fluids to 150% of calculated volume if necessary
Dire or emergency surgical procedure	Escharotomy Fasciotomy

5.1.1. Airway

5.1.1.1. Inhalation Injury

Inhalation injury is the most frequent cause of death in burns patients. [80, 81] It is a greater contributor to overall morbidity or mortality than either percentage of body surface area affected or age. It has been reported recently that the presence of inhalation injury increases burn mortality by 20%. [80] Children and the elderly are especially vulnerable due to their limited physiologic reserve. Aggressive diagnosis and early prophylactic intubation can be life saving. All patients with facial burn or burn in an enclosed space should be assessed by an anesthetist, and the need for early intubation ascertained before transfer to a specialized burn center. [82]

The clinical diagnosis of inhalation injury has traditionally rested upon high index of clinical suspicions, and a group of clinical observations. [83] The clinical warning signs observed include facial burns, singed nasal vibrissae, and a history of burn in enclosed space. Other tell-tale signs which should not be overlooked are changes in voice quality, hoarse

brassy cough, croup-like breathing, productive cough with or without carbonaceous sputum (sputum containing soot), inspiratory stridor, and respiratory difficulty with flaring of alar nasae, tracheal tug and rib retraction [83-85] Hypoxia, rales, rhonchi and wheezes are seldom present on admission, occurring only in those with the most severe injury and implying an extremely poor prognosis. [86]

Chest radiograph taken on admission for the diagnosis of inhalation injury is generally of little value in immediate burn assessment. [87] It does however, provide a good baseline investigation for evaluation of progress as almost two-thirds of patients with inhalation injury develop focal or diffuse infiltrates or pulmonary edema within 5–10 days of injury. [87] Fiberoptic bronchoscopy is the current standard in diagnosing inhalation injury. [84, 85] It identifies upper airway injury through observation of soot, charring, mucosal necrosis and airway edema. A positive or negative finding on upper airway injury however, does not reflect on the possibility of lung parenchymal injury. [85, 88] To evaluate lung parenchyma damage, Xenon scanning has been utilized to demonstrate areas of the decreased alveolar gas washout, which identifies sites of small airway obstruction caused by edema or fibrin cast formation. [89] Another more recent method of evaluating inhalation injury is the estimation of extravascular lung water by simultaneous thermal and dye dilution measurements. [90] This procedure has proved useful in separating parenchymal from upper airway injury.

Acute upper airway obstruction or supraglottic injury occurs in approximately one-fifth to one-third of hospitalized burn patients with inhalation injury and is a major hazard because of the possibility of rapid progression from mild pharyngeal edema to complete upper airway obstruction. [91] It is usually the clinical consequence of direct thermal insult to the upper airway as well as chemical irritation, especially during the first 12 h of injury. [72] The worsening of upper airway obstruction is marked by supraglottic structures edema with obliteration of the aryepiglotic folds, arytenoid eminences, and interarytenoid areas, which prolapse to occlude the airway. [92] Whenever a supraglottic injury is suspected, the most experienced anesthetist in airway management should perform endotracheal intubation. Securing the endotracheal tube can become increasingly difficult if not carried out immediately due to the rapid swelling that occurs within the next 72 h. [93] Acute upper airway obstruction is also exacerbated by systemic capillary leak, bronchospasm from aerosolized irritants, and decreased lung and chest wall compliances due to swelling or burn to the chest wall. [94-98] Although upper airway edema usually resolves in 2 to 3 days, it can continue to worsen and patient intubated for supraglottic injury should be monitored closely. Extreme care should continue be taken if these patients are extubated over the next 48 to 72 hours. [82]

The pathophysiologic changes in the parenchyma of the lungs that are associated with inhalation injury are not the result of direct thermal injury. Damage to the lung parenchyma or infraglottic injury is caused by the incomplete products of combustion which causes lower airways chemical tracheobronchitis and bronchospasms. [99] The small airway becomes occluded with sloughed from endobronchial debris and loss of ciliary clearance mechanism. Occluded segments of the lung causes increased intrapulmonary dead space and difficulty in gaseous exchange from intrapulmonary shunting, and interstitial and alveolar flooding. This predisposes the patient to serious infection of the already denuded tracheobronchial tree and poorly compliant pulmonary parenchyma over the next few days of admission. [94-98]

Many toxic gases in house or industrial fire are injurious to the lung parenchyma, in particular, the aldehydes and oxides of sulphur and nitrogen. [100, 101] The sulfates,

phosphates, and chlorides derivatives are acidic and induce rapid pulmonary edema, as well as systemic acidosis. Burning polyvinylchloride (PVC's) yields at least 75 potentially toxic compounds, including hydrochloric acid and carbon monoxide. [102] Patients with pre-existing reactive airway diseases are particularly vulnerable to irritative gaseous exposure.

The treatment for inhalation injury demands vigorous pulmonary toilet and ventilatory support to limit rapid lung deterioration. Airway clearance techniques are an essential component of respiratory management of patients with inhalation injury and it demands the involvement of respiratory therapists, nurses and doctors who play a central role in its clinical management. [103] Bronchial hygiene therapy is a term used to describe several of modalities such as therapeutic coughing, chest physiotherapy, early ambulation, airway suctioning, therapeutic bronchoscopy and pharmacologic agents to achieve this goal. [104-111]

Among the pharmaceuticals employed are bronchodilators and mucolytics. Bronchodilators have been employed with good outcome in many cases. [112, 113] Most of them act on the biochemical mechanism, which controls bronchial muscle tone. Aerosolized sympathomimetics are effective in relaxing bronchial muscle tone and stimulating mucociliary clearance. Racemic epinephrine is used as an aerosolized topical vasoconstrictor, bronchodilator, and secretion bond breaker. [104] Beta antagonists such as salbutamol may assist with exacerbation of reactive airway disease, which is very common due to the inhalation of toxins and particulate debris. [113] Water, employed as a diluent for racemic epinephrine, lowers both the adhesive and cohesive forces of the retained endobronchial secretions, thus serving as a bond-breaking vehicle. [104] Aerosolized N-acetylcysteine is a powerful mucolytic agent and has proved effective when combined with aerosolized heparin for the treatment of inhalation injury in animal studies. [108, 110] Heparin/N-acetylcysteine combination acts as scavenger for oxygen free radicals and improved patients mortality with reduced re-intubation rates and incidence of atelectasis.

5.1.1.2. Carbon Monoxide Poisoning

Combustion of carbon in an oxygen-deficient environment results in the production of carbon monoxide. [102, 114] Carbon monoxide is an invisible and odourless gas with nearly 200 times greater affinity for haemoglobin than oxygen. It competes with oxygen binding sites on the haemoglobin to form carboxyhemoglobin (COHb) and thus, reduces haemoglobin oxygen carrying capacity. The deprivation of oxygen at the tissue level is made worse by a concomitant leftward shift of the oxyhemoglobin dissociation curve. Because of its high affinity for haemoglobin, only a minimum level of carbon monoxide present in fires in enclosed space can cause significant carbon monoxide poisoning. Clinical findings of headache, nausea, and behavioral disturbances occur only at COHb level above 30%. [99] The pathognomonic cherry red skin discoloration is unreliable as a sign of carbon monoxide poisoning as it only occurs at COHb level above 40%. [99] Carbon monoxide poisoning can only be evaluated by measurement of serum COHb. [99] The level however, is a poor indicator of poisoning since most burn patients are placed on 100% oxygen on scene and upon arrival to emergency department. [115] The time from injury to measurement is very important, because it takes 4-5 h for levels to fall by one-half while patients breathe room air and less than 1 h on 100% oxygen. [99] Clark et. al. has developed a nomogram to estimate the original level of COHb at the time of extrication from the fire, based both on time from extrication and oxygen concentration delivered between time of extrication and time to first blood gas. [115]

Normal COHb levels are generally below 3% but can rise to 10-15% in heavy smokers. Levels below 10% are generally not considered harmful to the healthy person but can be deleterious in individuals with cardiovascular disease. As levels increase above 15%, symptoms such as headache and lethargy become common. At 30% and above, these symptoms are supervened by dizziness, nausea, and impaired vision, and unconsciousness develops at levels between 40% and 50%. Carbon monoxide poisoning at 60% and above is frequently associated with death.

Carbon monoxide can dissociate from hemoglobin, with the speed of dissociation determined by arterial oxygen content. Carboxyhemoglobin has a half-life of approximately 5 h in room air, reduced to 1 h in 100% oxygen, and further reduced at hyperbaric levels of oxygen at 3 atmospheres to approximately ½ hour. [99, 116] Therefore, all suspected or significant exposure to carbon monoxide should be treated with administration of 100% oxygen continued for several half-lives. It must also be remembered that the COHb level on arrival to the specialized burn center does not reflect the initial level of COHb at time of extrication from the fire because most of them would have received 100% oxygen on scene, before an arterial blood gas sample is obtained. Regardless, the first line management for carbon monoxide poisoning is usually supportive with application of 100% oxygen, either by facemask or by following endotracheal intubation.

The use of hyperbaric oxygen in the treatment of carbon monoxide poisoning is controversial. [116, 117] Physiologically, the rationale is clear as the half-life of COHb is reduced by almost 90% at 3 atmospheres compared with room air but a recent meta-analysis failed to support the use of hyperbaric oxygen therapy as a beneficial standard practice. [118] When considered against the backdrop of transferring a critically ill patient to a poorly accessible hyperbaric oxygen chamber and without a clear benefit of treatment, it is hard to justify its usage as regular practice.

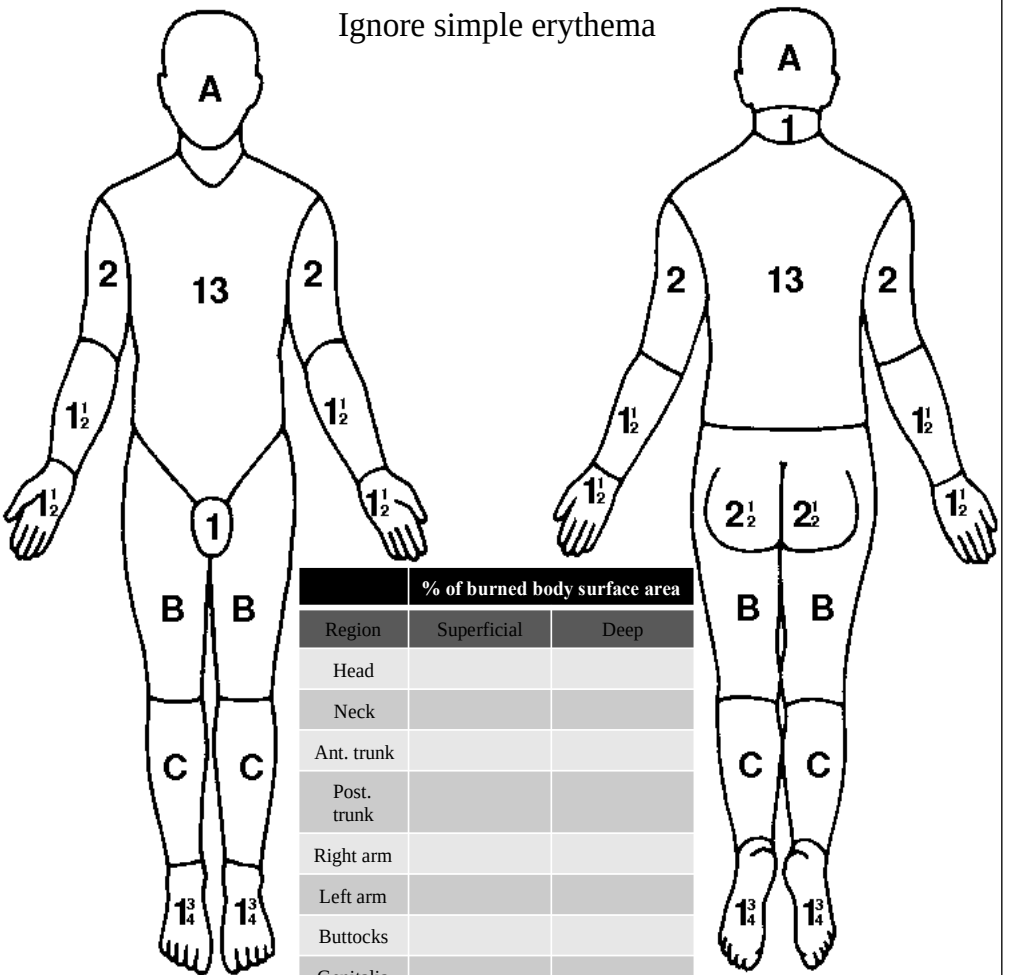
5.1.2. Burn Assessment

Burn should be debrided on initial assessment to allow determination of its depth. The European working party of burn specialists recommends cleaning burn with soap and water or disinfectant to remove loose skin, including open blisters. [119] The raised epidermis of bullae should be removed or deroofed, followed by excision of sloughed tissue. All blisters should be deroofed apart from the isolated lax blisters of <1 cm^2. [120] Although the clinical evidence for ‘deroofing’ of blisters is poor, without ‘deroofing’ burn depth cannot be adequately examined.

5.1.2.1. Burn Size

Burn size assessment is an important exercise during early burn management as it determines the amount of fluid, which the burn patient requires. There are a few commonly accepted methods to estimate the percentage of total TBSA burn, with some more practical than others in their use in emergency department or specialized burn center. The initial assessment of burn size should be performed with a standardized Lund and Browder chart (Figure 1). [121] It takes into account changes in body surface area with age and growth, therefore making it very useful across all age groups. It also has good interobserver agreement. Whilst Lund and Browder chart gives more accurate TBSA burn estimation, its use in pre-hospital setting is uncommon, and they are not, therefore, as widely used in non-specialized center. The simpler Wallace’s rule of nines is helpful for rapid assessment but less

accurate (Figure 2). [121] It tends to overestimate the percentage of TBSA burn by about 3%. It is taken to be the current standard technique for assessing burn area in pre-hospital setting, and hence the tool that most management decisions are based on.



	% of burned body surface area	
Region	Superficial	Deep
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	9 1/2	8 1/2	6 1/2	5 1/2	4 1/2	3 1/2
B = ½ of one thigh	2 3/4	3 1/4	4	4 1/2	4 1/2	4 3/4
C = ½ of one lower leg	2 1/2	2 1/2	2 3/4	3	3 1/4	3 1/2

Figure 1. Lund and Browder chart for percentage of total body surface area burn estimation.

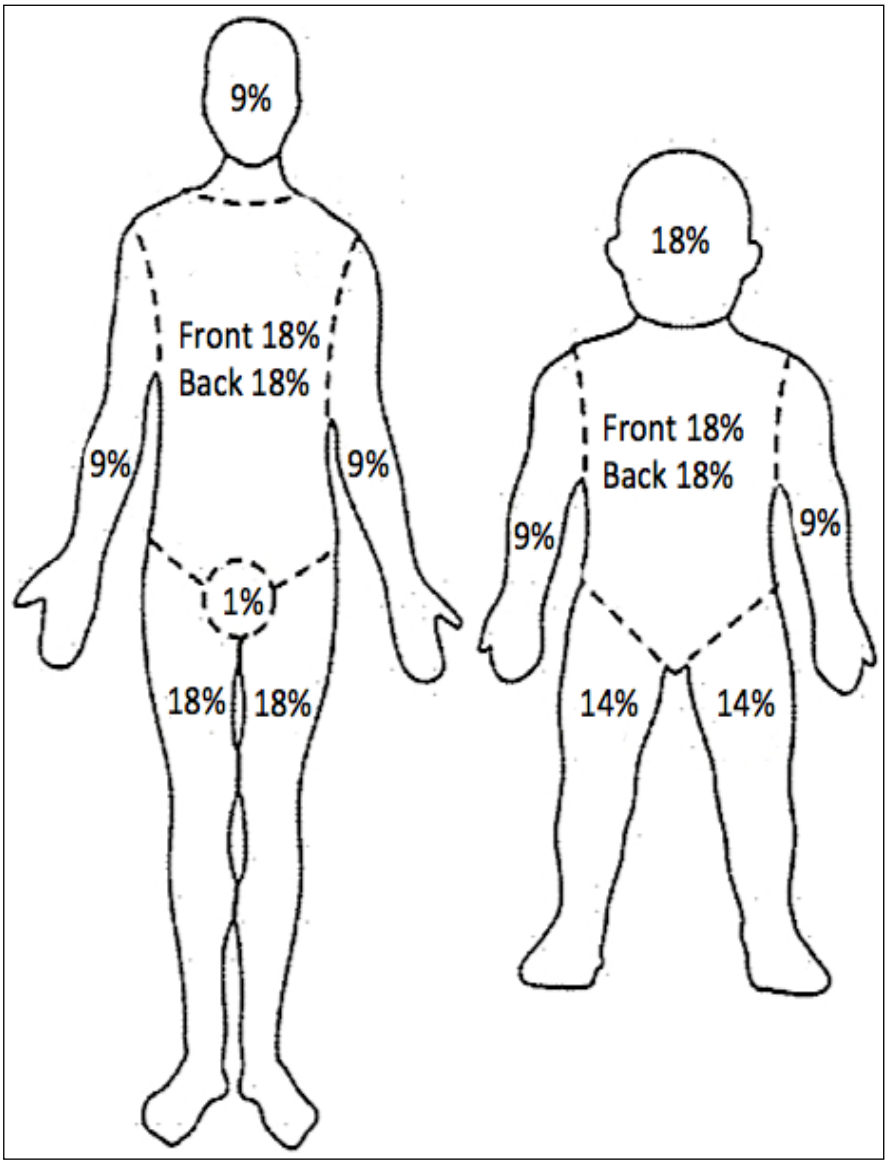


Figure 2. Wallace's rule of nines for percentage of total body surface area burn estimation. In children, the head and neck account for 18% and lower limbs 14% each. Note that for every year above one year old, the head decreases by about 1% and each lower limb gain about 0.5%. The adult proportion will be attained at 10 years old.

Another method of burn assessment is based on the palm being taken as a gauge of 1% TBSA. But studies of body surface area have shown that the adult palm with fingers corresponds to 0.8% of TBSA in adults and 1% in children. [122] This method is useful for estimating small burns (<15%) or large burns (>85%). In very large burns, the burnt area can also be quickly calculated by estimating the area of uninjured skin and subtracting it from 100. [123]

More recently, a serial halving method has been described. [124] This latter technique is effective in burn size estimation in pre-hospital assessment due to its rapidity and ease of use.

The approach is based on serial halves of >50%, <50%, 25–50%, or <25%. [124] When compared with rule of nines, it allows management decisions to be made that are equivalent to those that would have been made using the rule of nines. This is particularly valuable in pre-hospital assessment, where a key end point is appropriate disposal to further care. However, it is advocated that the serial halving method only be used as an initial assessment tool or with conjunction with other existing methods.

5.1.2.2. Burn Depth

Quantifying the depth of burn is an important initial step in the treatment of burn as the attending surgeon weighs on the decision for resuscitation, transfer, and surgical debridement. [125] A common mistake in burn depth assessment in the inexperienced is inclusion of erythema. Only de-epithelialized area should be included in burn assessment calculation. Although it is ideal to assess burn depth accurately in emergency situation, the distinction between superficial and deep partial dermal burns is not always precise and burn wound may not be homogeneous with respect to depth. Clinical estimation of burn depth is often a subjective process with independent blinded comparison among experienced surgeons showed only 60-80% concurrence. [126] Fortunately, a detailed formal depth assessment is not necessary for partial thickness burn, as the distinction between superficial and deep partial thickness dermal burns is based largely on their healing times. Under normal circumstances, superficial partial thickness dermal burns do not require surgery and heal within 10–14 days by epithelialisation without scarring. [119, 127] Deep partial and full thickness dermal burns take longer to heal and are likely to scar. Deep partial thickness dermal burn requires excision and skin grafting. A retrospective cohort study by Cubison et. al. examined 337 children with up to a five year follow-up found hypertrophic scarring occurred in less than 20% of superficial scalds that healed within 21 days but in up to 90% of burns that took 30 days or more to heal. [127] In order to achieve good aesthetic outcomes, all partial thickness dermal burns that have not healed by 10-14 days should be referred to a specialized burn center. [119]

In superficial partial thickness dermal burns, the layer of necrosis occupies only the upper (papillary) dermis, with normal underlying reticular dermis. Clinically, such burns are pink or red, may have blistering, are painful, and have a good blood supply. These are usually managed conservatively without excision and grafting. In contrast, in deep partial thickness dermal burns, the layer of necrosis extends into the reticular dermis, with the zone of stasis extending deep into the dermis. Clinically, these burns tend to be less red with poor blood flow. Table D summarizes the key characteristic of various burn depth appearances as outlines in EMSB course. [72] It is important to be aware that burn wounds are dynamic and need reassessment in the first 24-72 hours because the depth can increase especially if inadequately treated or infected. [72] There have been various methods described to improve the accuracy of burn depth assessment but the high outlay costs for these equipments preclude their use outside specialized burn centers. For example, laser Doppler imaging, which assesses skin blood flow, has 90-100% sensitivity and 92-96% specificity for estimating burn depth when compared with clinical assessment and conventional histopathology. [126] Other methods such as transcutaneous videomicroscopy (direct visualization of dermal capillary integrity) and infrared thermography (temperature gradient between burnt and intact skin) among others are still largely experimental to date. [128, 129]

Table D. The key clinical features that distinguish the different level of burn depth

Depth	Color	Blisters	Capillary refill	Sensation	Healing
Superficial	Red	No	Present	Present	Yes
Superficial partial thickness dermal	Pale pink	Small	Present	Painful	Yes
Deep partial thickness dermal	Dark pink or blotchy red	+/-	Absent	Absent	No
Full thickness dermal	White	No	Absent	Absent	No

5.1.3. Circulation and Resuscitation

Thermal burn injuries pose a significant local and systemic insult. The presence of burn is associated with significant fluid loss due to the damage and loss of protective keratin layer of the skin and their systemic reactive changes. Effective fluid resuscitation remains the cornerstone of management in major burns. It is widely accepted that one of the principal factors responsible for the reduction in mortality from acute burn was the introduction of fluid resuscitation. In the UK, expert consensus recommends that fluid resuscitation be initiated in all children with 10% burns and adults with 15% burns (Table C). [14, 78] Fluid replacement should also be started on scene for burn >25% TBSA and/or if time to hospital is more than one hour from the time of injury. Children who had fluid resuscitation within 2 h had a lower incidence of sepsis, renal failure, and overall mortality. [14, 72]

Over the years, several formulas based on body weight and area burnt, estimate volume requirements for the first 24 h. Although none is ideal, the Parkland formula and its variations are the most commonly used (Table C). [130] The aims are to maintain vital organ perfusion and tissue perfusion to the zone of stasis to prevent extension of tissue necrosis. Although multiple studies have reported the inadequacy of standard fluid resuscitation formula, with needs routinely exceeding the calculated requirements, this is likely due to variations in body mass index, accuracy of the calculated size of burn, and differences in mechanical ventilation. [131-133] It may also be that none of the present protocols are ideal because simply that different protocol suit different patient in different situation.

The preferred resuscitation fluid varies greatly. This is reflected by the evolving protocols for resuscitation from the plasma infusions of the 1940s to crystalloid resuscitation using the Parkland formula-guided Hartmann's infusion today. [134-136] There is no robust scientific evidence to support the adoption of one particular protocol over the rest. Many believe that resuscitation fluids should be isotonic for the first 24 h, and then colloid added after 24 h, when capillary integrity returns. [130, 137, 138] Although in theory, the addition of colloids in burn resuscitation may decrease total volume requirement, randomized controlled trials are still needed to evaluate its full benefits. [139] A recent Cochrane meta-analysis of 65 randomized controlled trials of trauma, burns, and post-surgery patients found no evidence that colloid resuscitation reduces mortality more effectively than crystalloids. [140] Currently, the most popular type of fluid is crystalloid Hartmann's solution, which effectively treats hypovolemia and extracellular sodium deficits. [130, 137] Many burn centers continue to add colloid after the first 12 h for large burns. [141] Sodium chloride solution (0.9%) should be avoided because it causes hyperchloremic metabolic acidosis. [142] A recent survey of burns centers in USA and Canada revealed that 78% of centers used the Parkland formula to

estimate resuscitation fluid volumes and that Ringer's lactate (similar to Hartmann's solution) was the most popular type of fluid. [137] In UK and Ireland, the estimated resuscitation volumes were also calculated using the Parkland formula in 76% of units, and Hartmann's solution remained the most widely used. [130] Minor burns (<15-20%) need 150% of normal maintenance intravenous fluids. [143-145] Approximately half of the centers did not routinely change the type of intravenous fluid administered after the initial period of resuscitation. [130] Resuscitations were discontinued after 24 h in 35% of centers and after 36 h in 30% of centers. [130]

Resuscitation starts from the time of injury, and thus any delays in presentation or transfer to the hospital or specialized burn center should be taken into account, and fluid infusion rate calculated accordingly. The goal of resuscitation is to achieve enough volume to ensure end organ perfusion while avoiding intra-compartmental edema and joint stiffness. Care should also be taken not to over-infuse small, frail, elderly patients with a history of left ventricular failure (LVF). Resuscitation formulae are only guidelines, and the volume must be titrated against monitored physiological parameters such as urine output, lactate, base excess, peripheral temperature, blood pressure, and heart rate. [146, 147] In UK, it is recommended that adults with burn >20% TBSA and >15% TBSA in children requires burn resuscitation monitored with urinary catheter for adequate urine output (Table C). [72] Patients with pre-existing conditions that may affect the correlation between volume and urine output require invasive monitoring for circulatory end points such as mean arterial blood pressure, central venous pressure, and if a pulmonary artery catheter is placed, pulmonary artery wedge pressure. [132, 146, 147] Central venous pressure or pulmonary capillary wedge pressure should be considered in patients with known myocardial dysfunction, age greater than 65 years, severe inhalation injury, or fluid requirements greater than 150% of that predicted by the Parkland formula. [144]

5.1.4. Dire or Emergency Surgical Procedure

Any deep partial thickness or full thickness dermal burns that encompass or almost encompass a region of the body can form a tight tourniquet as a result of eschar formation which limits tissue elasticity and excursion. [72] On initial examination, there may be no signs of compromise, but with the development of edema from the burn injury and fluid resuscitation, problems will eventually be compounded through the combination of external splintage and internal structural compression. As edema in the region continues to worsen, this tourniquet effect is enhanced. In the extremities, it will deprive the limbs of blood supply by the circumferential banding of eschar. Any burns involving extremities must be checked for circumferential burn and compartment syndrome. [72] The release of a restricting eschar and sometimes, fasciotomy will improve perfusion of distal extremity.

As the resuscitation continues, chest and abdominal walls may also become edematous. This causes constriction to the trunk that makes ventilation more difficult especially in patients with an already compromised, direct pulmonary injury. Ventilation insufficiency is due to the presence of burn eschar on the chest, forming a tight cuirass that restricts movement of the chest wall. These truncal constrictions require rapid and complete escharotomies to allow the underlying viable tissue to springs through the eschar and facilitate respiratory excursion. Often, circumferential burn of the neck, especially in children, can worsen respiratory embarrassment due to unyielding eschar that externally compresses and obstructs the airway. Escharotomy to the neck will be helpful in reducing the tight eschar

and therefore, decrease the pressure exerted on the trachea. The elevated intra-abdominal pressure reduces the excursion of the diaphragm causing diminished functional reserve capacity of the lung. Raised abdominal compartment syndrome also has a negative impact on splanchnic, renal, and limb perfusion.

Theoretically, escharotomy should be a painless procedure, requiring no anaesthesia. It is rare for a burn to be full thickness in its entirety and yet, having areas of partial thickness loss, which are exquisitely painful. Escharotomy bleed profusely and need to be performed in a monitored environment equipped with electrocautery and conscious sedation. [79] For this reason, it is a good practice to infiltrate the proposed line of incision with a solution of 0.5% lignocaine with 1:200,000 epinephrine (maximum dose of 7 mg/kg), leaving it for at least 10 min before incising. The addition of hyalase (1500 iU per 50 ml) to the solution will improve penetration of the eschar. The incision should extend into normal tissue in both extent and depth, with the healthy tissue bulging through the release, forcing the eschar apart. Fasciotomy may also need to be undertaken in patients with deep burn, or those caused by high voltage current. Fasciotomy for release of edematous muscle should be performed in controlled environment such as in operating room to allow for appropriate visualization of the anatomy. [79]

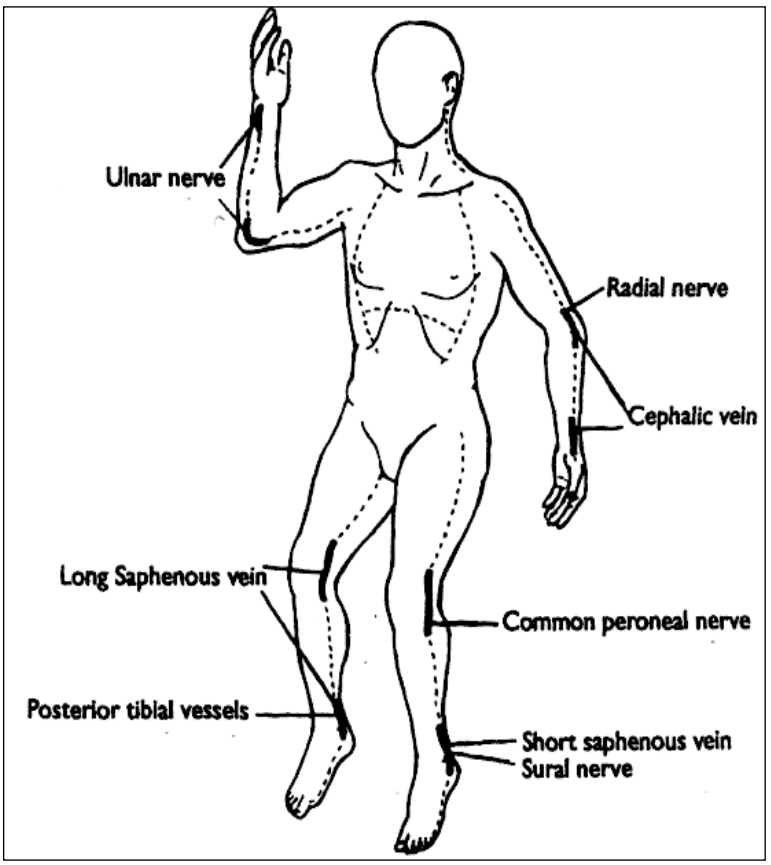


Figure 3. Sites of escharotomy incision with particular attention over areas where vital nerves and vessels are adjacent to the site of incisions.

Although escharotomy may be needed to avert respiratory distress or vascular compromise of the limbs from constriction in full thickness circumferential burns involving the neck, chest, abdomen, or limbs, a proportion of patients will have no signs of any compromise to circulation or ventilation. In these cases, escharotomies should be performed prophylactically if they are to be transported any distance without ability for regular monitoring or to act on clinical findings. In the limbs, prophylactic escharotomy has been proven to be beneficial. [104] Whilst the value in the fingers is controversial, a controlled study demonstrated a statistically significant number of phalanges were salvaged in circumferentially burned fingers with early escharotomy. [148]

Care should be taken in the placement of incisions for escharotomy to insure adequate release and to avoid damaging vital structures such as nerves and vessels. The concept and techniques for escharotomy and fasciotomy have been well described by Burd et. al. based on the fundamentals of decompression. [149] Figure 3 illustrates in brief, the position of escharotomy incisions as taught in EMSB course in UK. [72]

5.2. Analgesia

The pain threshold temperature for skin is 42 ^{o}C. [20] Control of burn pain must begin upon initiation of medical care. As previously indicated, analgesia is best accomplished by cooling and covering the burned area. [4] Once intravenous access is gained and resuscitation started, intravenous opioids should be administered. Intravenous morphine is the first line of acute pain management in burns (Table C). Its effect is immediate with peak analgesia at 10 min. The recommended intravenous dose for adult is 1–2 mg repeated every 3–5 min, and 20 mcg/kg repeated every 3–5 min in children above one year old. [150] The opioid dose occasionally exceeds the standard weight-based recommendations and is necessary to achieve adequate pain control. Intravenous opioids can be titrated to make the adult patient more comfortable and should be accompanied by an antiemetic. There is no evidence that opioid addiction occurs more often in burn patients than in other populations requiring opioids for acute pain (approximately 1 in 3000). [151] Oral opioids can also be administered in adults if no intravenous access obtained. Entonox should only be used when these options are unavailable as it may be difficult to administer, has varying efficacy, and decreases the oxygen delivery. It is typically self-administered by an awake, cooperative patient via a mouthpiece or face mask in a concentration of 50% nitrous oxide and 50% oxygen. [152] In children intranasal diamorphine is another alternative option that may be considered. [153, 154]

5.3. Antibiotic Usage

The use of systemic prophylaxis antibiotic in burn is controversial. In the acute setting, Ravat et. al., through their review recommended that systemic antibiotic prophylaxis could be used in patients needing invasive surgery but not in those for dressing changes. They recommended oxacillin or cloxacillin (30 mg/kg) or first generation cephalosporin (30 mg/kg) to target methicillin-sensitive Staphyllococcus. In case of allergy, clindamycin should be used (10 mg/kg). [155] Another recent systematic review and meta-analysis by Avni et. al.

reported that systemic antibiotic prophylaxis, given for 4 to 14 days after admission, cut all-cause in-hospital mortality by 46%. [156] But the authors cautioned that none of those findings are definitive as the overall methodological quality of the studies were poor. Other available data from adult, paediatric and mixed population studies have demonstrated that systemic antibiotic prophylaxis in burn patients has no role in the prevention of bacterial infections. [157-164] There has also been a paucity of evidence on the relevance of post-operative antibiotic use in the management of paediatric burn and with the lack of support of the role of prophylactic antibiotic in the surgical management of paediatric burn, there seems to be a diminishing role of peri-operative antibiotic use. [157, 159, 160, 165-167] Peri-operative antibiotic prophylaxis has not been shown to decrease the incidence of graft or donor site infection. [168] There has been significant evidence that antibiotic therapy prescribed to prevent infection of burned skin did not actually prevent it and even facilitates the emergence of multi-resistant bacteria. [163] It is likely that diffusion of antibiotic in the burned skin is questionable and cannot achieve bactericidal concentrations so that bacteria can grow and develop resistances. The compromise to skin barrier and the overgrowth of bacteria in the burn eschar leading to sepsis have led to a high rate of antibiotic resistance in common organisms.

On the other hand, early application of burn with topical antimicrobial has been shown to decrease the bacterial overgrowth and incidence of burn wound sepsis. Topical antimicrobials also keep the wound moist and control pain. Local burn wounds management with topical agents has a well documented efficiency in both preventing and treating burn infections. [169] Current treatment regimens include silver sulfadiazine, Bactroban, or Sulfamylon in conjunction with daily cleaning and debridement. Its use however, is no substitute for a timely surgical intervention. Without eventual surgery, the benefit of topical antimicrobial preparations on mortality is only minor on burns less than 40% TBSA. [170]

Patients who show signs of sepsis should receive a complete work-up, with a special focus on the most commonly encountered bacteria in burn centers, including Staphylococcus aureus, enterococci and Pseudomonas aeruginosa. [171, 172] Diagnosis of infection in burn patients is not easy because clinical and biological infection criteria are poorly relevant, especially in heavier burn patients. Clinical parameters such as hyperthermia, hyperleukocytosis and increased C-reactive proteins can be part of physiological reactions to large thermal insult. A large burn triggers a systemic inflammatory response syndrome (SIRS), which mimics usual clinical and biological signs of infection. [173] Children with significant burn can often have moderate fever in the absence of infection and in this circumstances, administration of broad-spectrum antibiotic is not appropriate and may ultimately worsen outcomes in previously uninfected children. [166, 167] There has been insufficient data to show judicious use of antibiotics in febrile paediatric victims is unacceptable. As long as the infection is not documented, antibiotic therapy is empiric. Therefore, broad-spectrum antibiotics should be chosen for maximum efficacy. In established burn wounds sepsis, targeted antibiotic usage is helpful to eradicate the bacteraemia or septicaemia, and reduces mortality rates. [167]

5.4. Wound Care

The vast majority of burns in Europe are treated by non-specialists in the community or general hospitals. Of the 2000 people per million who suffer from burns per year, most are managed by inexperienced healthcare professionals. [119] Although a careful guideline on criteria for referral and transfer to a burn center allows safe treatment of most burn cases outside of regional burn centers, the significance of burn wounds management with regular follow up cannot be overemphasized. Burn wounds management warrants continuity of care in the part of both, the managing physicians or the specialists. Although immediately after assessment, a simple non-adhesive dressing, such as soft silicone (e.g. Mepitel®), padded by gauze is sufficient in most small superficial and superficial partial thickness dermal burns, deeper dermal burn dressings require significant knowledge of the science of dressings. One of the keys to successful burn wounds management is the choice of appropriate dressings to provide a moist and clean wound environment. Factors previously thought to influence time to wound healing, such as percentage burned, sex, age, and infection, were not found to be as significant in a study by Jewell et al. [174]

The general principles of a good dressing is that it should maintain a moist wound environment to aid healing. [119] The provision of a moist environment does not remove the need to prevent the accumulation of excessive moisture that can lead to skin maceration, delayed wound healing and infection. Therefore, an ideal dressing should also have sufficient capacity to absorb excess exudate. Dressings should also provide an effective barrier to the exterior to reduce the risk of infection, easy to apply and fit well to the contours of the skin to maintain maximum contact with the wound, and non-adherent to the wound to ease pain and dressing changes.

The principle of moist wound healing is well established, and has been shown to accelerate the healing process with less pain and inflammation. [175, 176] A broad knowledge of the characteristics, strengths and weaknesses of both modern and traditional dressings are essential to aid clinical decision-making to optimize burn wounds management. Often, the choice of dressing is also influenced by local availability and personal preference of the physician. Wound dressings have changed considerably over the past 4–5 years and many different wound dressings are now available across Europe. [119] Modern wound dressings, utilising hydrocolloids, Hydrofiber®, silicones, alginates and polyurethane, fulfil many of the essential and desirable criteria of an ideal dressing. The use of silver-impregnated modern dressings is now also becoming more widespread in both general hospitals and specialized burn centers. The traditional dressings, such as paraffin gauze and silver sulfadiazine, are used less often nowadays as they can cause wounds to dry up and do not effectively support optimal healing. [177] They may also allow microorganisms to access the wound, leading to increased risk of infection. [178]

Although topical antimicrobials are proven to be beneficial in burn wounds management, other topical dressings used include everything from honey to silver sulfadiazine to duoderm. [179-184] Among the antimicrobial agents used, many have silver component such as silver sulfadiazine (cream), Acticoat (fabric), and silver nitrate (solution). Silver has bactericidal activity that reduces inflammation and promotes healing. [181] Silver sulfadiazine cream is soothing and can be used for deeper dermal burns. Acticoat is a silver-impregnated material dressing that provides antimicrobial coverage for 3 to 7 days. Another compound, cerium nitrate, is a heavy metal that is still under investigation as a topical agent. It has been shown

to be a promising agent with survival advantage data of patients matching those that underwent early surgical intervention. [185-190] It demonstrates the ability to bind lipid protein complexes that are responsible for SIRS without binding to collagen or albumen in normal skin. [189, 190] Cerium nitrate solution is not an easy compound to administer and lacks some of the analgesic properties of silver sulfadiazene. A mixture of the two compounds, Flammacerium, is now commercially available.

As burn is a dynamic process, dressings should be changed and wound examined at 48 hours to reassess its depth. [12, 72] Dressings on superficial partial thickness dermal burns can be left for three to five days before the next change of dressing. If evidence of infection exists, daily wound inspection and dressing change is necessary. Deep dermal burn wounds need daily dressing until the eschar has lifted and re-epithelialization started. Depending on the level of healing and type of dressing, a wound dressing can stay on the burn wound for 10 days, unless there are specific reasons that might require wound inspection and dressing change. [119] Leaving a wound dressing in situ has the advantages of improved patient comfort, reduced unnecessary nursing time and controlling the cost of regular dressing change. There is little benefit to be derived from frequently checking the progress of a partial thickness burn before the day 10. [119]

5.5. Transport

There are a number of published guidelines and requirements concerning the transport of the critically ill and injured. [191, 192] These should be used in devising local policies with the inclusion of specific requirements of burn patients as laid down in EMSB course. [193] Of primary importance is the need to avoid any delay in the transfer of someone with burn injury to a place of definitive care. All treatment should be carried out with the aim of reducing on scene times and delivering the patient to the appropriate treatment center. This should be the nearest appropriate emergency department, unless local protocols allow direct transfer to a specialized burn center. The use of retrieval teams and/or aeromedical transfer needs to be balanced in each case. Communication with the recipient hospital should give essential information only such as age, sex, incident time and mechanism, ABC problems, relevant treatment received and expected time of arrival. [3, 194-198] Important issues to also consider when transporting children with serious burn include maintenance of body temperature, fluid administration if transport time >1 h, accurate documentation, notification of family, and identification of the child's legal custodian. In some cases, the possibility of non-accidental injury should also be borne in ones mind. It is recommended by the National Burn Centre Response Committee (NBCRC) in UK that all complex burns referred for admission reach the specialized burn center within 6 h of injury across the British Isles and within 4 h of injury if referred from an urban site. [3] A failure to achieve these targets should be regarded as a critical incident and the reasons investigated.

6. SURGICAL DEBRIDEMENT

Despite appropriate antibiotics and dressings, some patients with large burn, who are cardiovascularly stable and well resuscitated, succumb relatively early. Topical antimicrobials are frequently viewed as a panacea in burn wound management. Whilst topical agents such as silver sulfadiazine cream can control toxic shock in scalded children, they are not a substitute for timely surgery. Patients with partial thickness burns continue to exhibit symptoms of SIRS leading to multi-organ failure in the largest injuries. [170] Although infection at the interface between burn eschar and viable tissue may contribute, a systemic effect of dead burnt tissue seems responsible for the eventual demise of these patients. The ability of burnt skin to kill has been demonstrated in mice by injection of fractionated homogenates of burn eschar, in a dose dependant manner. [199] A rodent experiments have demonstrated that the degree of immune upset is quantitatively linked to the amount of burnt tissue present, and that sub lethal quantities can effectively suppress the immune system, making the animal prone to infection. [200] For these reasons, early excision of burns has been advocated, and shown to be the single most important factor in reducing mortality from burns over the last quarter century, particularly in patients over 50 years of age. [201]

Cope et. al. popularized the concept of early excision and autografting of burns after treating patients from the Coconut Grove fire in Boston in 1942. [202] With the advent of topical burn dressings and antibiotics, surgical excision of burns fell out of favour. Instead, burns were treated with prolonged dressing to lift the eschar before surgical intervention. Janzekovic renewed interest in early excision in 1970, when she reintroduced the concept of tangential excision of the necrotic tissue and immediate closure with split thickness skin grafts. [203] Ong et. al. performed a meta-analysis of data from six randomized, controlled trials, published from 1966 through 2004, that compared early excision of burns with wound dressing and grafting after eschar separation. [204] They found a trend toward a reduction in mortality with early excision with only 22% treated with excision died in contrast to 62% in those treated with wound dressing and delayed grafting.

The role of early debridement and/or skin grafting is also advantages in the management of paediatric burns. In a retrospective study, Xiao-Wu et. al. examined 157 children with burns involving ≥40% of TBSA who were stratified according to the number of days between the injury and the first operation (0 to 2, 3 to 6, or 7 to 14 days). [205] Delayed excision and grafting were associated with longer hospitalization and increased rates of invasive wound infection and sepsis in the group undergoing surgery 7 to 14 days after burn. Another retrospective study in 1988 investigated the mortality of 1674 children with burns and found that mortality was substantially reduced by prompt eschar excision. [206] These studies demonstrated that better survival and reduced length of hospital stay can be achieved with early excision in paediatric burns. [165, 206]

Excision of burn removes a principal nidus for bacterial infection and exposes a viable bed for skin grafting. Grafting minimizes fluid loss, reduces metabolic demand, and protects the wound from harbouring infectious organisms. Early excision and grafting have been shown to reduce inflammation, as well as the risks of infection, wound sepsis, and multi-organ failure. [204] Appropriate treatment must therefore be instituted early and infection prevented to encourage rapid healing. If the depth of the burn is unclear, the eschar can occasionally be left to lift off by itself, such as in the case of the ear or digits. For mixed-

depth wounds, topical therapy for 5 to 7 days will facilitate any spontaneous wound healing that may occur. In deeper burns, topical agents are only limited to maintenance of the wound until definitive treatment can be undertaken. Declaration of the depth of burn during that time, with frequent assessment of wound progression, should guide surgical planning. For deep partial and full thickness dermal burns, early identification, excision, and grafting of the wounds help avoid wound sepsis, decrease systemic inflammation, and improve outcomes in wound healing. It reduces the risk of long term complications such as hypertrophic scarring and burn contractures. Ideally, surgery should be performed within the first week after burn in a clinically stable patient. [207]

The goal of early excision is to remove all devitalized tissue and prepare burn wound for skin grafting. All necrotic tissue needs to be removed in order for the applied skin graft to engraft successfully. Tangential excisions are performed with a Goulian blade for small areas or those with multiple irregular contours (e.g. hand or knee) and a Watson blade for larger areas. These specialized blades with large guarded knives allow good control of the thickness of the excision. Sequential excisions of layers of burned tissue are carried out until a viable wound bed achieved, as evidenced by capillary bleeding, or continued down to healthy dermis, fat, muscle, paratenon, or periosteum. An alternative is to excise the burned tissue with underlying subcutaneous fat down to fascia, most commonly with the use of cautery. This approach is faster, requires less skin grafting, and results in less bleeding but can result in severe cosmetic deformity and reduced sensation because of the excision of cutaneous nerves. The wound may then be covered with an autograft, allograft, or synthetic skin substitute. If a healthy recipient bed is not available, other reconstructive options should be considered. In the case of deeply burned cartilage or bone, all devitalized tissue should be removed as soon as the patient's condition is hemodynamically stable and the fresh wound covered with skin, muscle, or myocutaneous flaps, as indicated.

One of the most important complications of excision and grafting is bleeding, which can be substantial. It is estimated as up to 100 to 200 ml of blood loss for every 1% of TBSA that is excised. [208-211] Operative methods to minimize blood loss during surgical debridement include performing excision early in the post-burn period, using cautery for fascial excision, injecting diluted epinephrine below the eschar, and excising extremities' burn under tourniquet. [209] The systemic response to burn is responsible for the significant blood loss secondary to an alteration in the coagulation cascade. Blood loss in burn surgery therefore, is greater during excision of colonized burns, and least if excised within 24 h of injury before significant wound angiogenesis develops. [212, 213] Although tangential excision can require extensive transfusion products, fascial excision usually does not due to easier control of bleeding vessels. In tumescent technique, the fatty tissue under the burns can be infiltrated with a solution of dilute epinephrine in saline until the tissue is distended and has a smooth, firm texture to reduce the severity of bleeding during excision. It has been shown that the use of tumescent epinephrine infiltration significantly limits blood loss. [214-217] For burns on a limb, a tourniquet can be placed to further limit bleeding during excision. [214] Other hemostatic methods such as the use of spray or sponge-soaked thrombin, topical epinephrine, vasopressin, fibrin sealant, and intravenous recombinant factor VII, can also reduce bleeding. [208, 211, 215, 218-220]

To achieve a safe outcome from large burn excision, a patient should be well perfused and operated in surgical theatre with well-controlled environment and active rewarming facility. When accompanied by acute normovolemic hemodilution and auto transfusion, large

burns can be excised immediately, safely and with minimal resources. [221] This should represent the gold standard in burn surgical care. [222]

For large wounds, once hemostasis has been achieved, a split-thickness skin graft can be applied. Autografts include full-thickness skin grafts, split-thickness skin grafts, and cultured epithelial cells. Full-thickness skin grafts are rarely used in burn surgery because of the added tissue loss. Split-thickness skin grafts allow for regrowth of the donor site with minimal scarring. Thin pieces of skin, consisting of epidermis and superficial (papillary) dermis, are harvested from a non-affected area, often the anterior thigh or abdomen, with the use of a powered dermatome at a thickness of 0.2 to 0.5 mm (0.008 to 0.020 inch). These split-thickness skin grafts are placed over the debrided area and secured with sutures or staples.

The success of skin grafts depends on not only surgical technique but also post-operative care including postoperative dressings and frequent assessment of graft viability. Simple dressings with petroleum gauze or non-adherent dressings, with or without antimicrobial ointment, have been used as dressing for skin graft with good outcome. Outer dressings on skin graft are designed to apply mild pressure to the graft to promote apposition of the graft and wound bed, and immobilize the graft to prevent shear forces from shifting the graft on the wound bed. Recently, fibrin glue or spray has also been used to improve adherence of both sheet and mesh skin grafts. [223] Grafts to the lower extremities can be protected by using double bandage wraps and those on the upper extremities especially the fingers, can be protected with an elastic wrap such as Coban. Skin grafted areas are regularly monitored for hematoma, seroma, and infection. Any fluid collection underneath the grafts should be evacuated immediately to promote adherence of the grafts to the recipient sites. Any necrotic areas should be sharply debrided. Infected grafts are aggressively treated with topical antimicrobials. After 4 or 5 days of surgery, a viable or taken graft can be mobilized with patient commenced on physical and occupational rehabilitation as appropriate. Any areas of graft loss can be debrided, and either re-grafted or allowed to heal by secondary intention.

The donor site heals spontaneously over a period of 1 to 2 weeks, depending on the age of the patient and the size of the donor site. Skin graft depth harvested should be tailored to pediatric or geriatric populations due to their thinner reticular dermis layer. The donor site from thinner skin grafts heal faster with less scarring, while thicker grafts provide more durable coverage but with more significant scarring at the donor site. The wound dressings for skin donor sites, which vary among centers, include petroleum gauze, alginate, and silver foam. Donor sites can often be re-harvested after about 2 weeks.

In large burns where insufficient donor sites are available, split-thickness skin graft can be meshed with variable ratios or it can be simply fenestrated to allow minimal expansion of coverage areas. In meshed grafts, it can be expanded by up to six times the original area. Fenestrating or meshing of the skin graft has several advantages including expanding the square centimeters of coverage, allowing for drainage of fluid from under the graft, and allowing for placement of the graft over contoured areas such as those with contour deformity. One of the disadvantages of the meshed skin graft includes a permanent weave-like appearance of the healed recipient site. Sheet skin grafts have a smoother healed appearance but need to be checked frequently for hematoma and seroma formation, and cannot be used for large burns where donor sites are scarce. If the burn is so extensive that there are minimal viable areas of donor skin, allograft such as cadaver skin or a dermal substitute may be used. Recently, cultured epithelial autografts are grown from patient skin samples. Seventy-five square meters may be grown from a 1 cm^2 specimen. However, few

centers have large success with cultured epithelial autografts secondary to lack of take and poor long-term durability. [224] Cultured skin substitutes consist of a tissue-engineered combination of dermis and epidermis have so far, not been approved by the Food and Drug Administration in USA. [225] In Europe and Australia, epidermal replacement techniques including cultured epidermal autografts and epidermal sprays are just becoming acceptable for clinical use. [225, 226] Its widespread use however, is limited by its higher rates of infection, longer preparation time and higher cost than traditional skin grafting. [227, 228] Although many of these new techniques show great promise, there is no consensus among experts about the optimal use of these products.

CONCLUSION

Care to the burn victims by healthcare professionals begins on scene or on first contact to pre-hospital management before arrival to the emergency department. Emergency burn management should follow guidelines as set up by Advanced Trauma Life Support (ATLS) and Emergency Management of Severe Burns (EMSB) to optimize patients' outcome. Criteria for referral and transfer for severely burn patients to specialized burns center should be adhered to allow satisfactory emergency care with its ancillary procedures and essential future rehabilitation. Many healthcare professionals continue to require continuous education to facilitate adequacy of their performance in caring for these patients. Awareness of first aid care to burns and subsequent wound management in minor burns should be emphasized to healthcare professionals in general hospital and primary care setting. The ever-evolving field of emergency care for burns continues to require their active participation in providing first line service to the general public. The importance of adequate emergency burn care and contributions made by primary healthcare professionals in the management of burns cannot be overemphasized as they are vital gatekeepers to the outnumbered, specialized burns centers in the world.

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Chapter 2

ADVANCEMENTS IN BURN THERAPY: PROMISE OF NANOMEDICINE

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ABSTRACT

Successful burn therapy remains to be a challenge in respect to its remaining scaring and functional and cosmetic outcome. The enhancement of dermal and epidermal regeneration is the ultimate aim in burn treatment. Recently, several promising lines for improved burn therapy have been proposed, with the focus of this review being on nanotechnology and nanomedicine-based systems. An ideal system should achieve permanent skin regeneration within both dermal and epidermal tissues, and provide good functional and aesthetic characteristics. Topical formulations destined for administration onto the skin need to posses optimal mechanical properties (such as spreadability), bioadhesion, acceptable viscosity and controllable release of active ingredients. The review discusses the current status, potentials and limitations for several of most promising research lines within the area of nanotechnology and nanomedicine. In addition, the use of *in vitro* and *in vivo* models as evaluation tools for nanomedicine destined for burn therapy is discussed.

INTRODUCTION

Successful burn therapy represents a specific challenge in respect to therapeutic outcome, scaring, and functional and cosmetic consequences. In an estimated number of patients suffering from burns annually, Brigham and McLoughlin (1996) suggested the number to exceed 2 million. It is probably an underestimate, as many patients will not seek medical help for minor burns or will rely on traditional ethnic remedies. The severity of the incidence can be seen in the number of deaths (5,000) from burns each year (only in USA; Demling, 2008).

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Although the complex arrays of cellular and molecular mechanisms involved in wound healing are rather well understood, the clinical results are still not confirming the improved knowledge on healing mechanisms. Wound healing, even when not impaired, results in a structurally and functionally satisfactory, but not identical, outcome (Li et al., 2007). In addition, more and more patients are diagnosed with complications in wound healing.

Conventional wound therapy involves the use of topical agents to clean, disinfect and stimulate healing. This is very often a painful process linked to high degrees of morbidity.

This review is an attempt to address the progress in nanotechnology and nanosciences, particularly nanomedicine, and their corresponding consequences on wound therapy.

When discussing modern wound dressings, very often, the first question arises on how far have we moved from the ancient medicine concept of treating wounds. The concept of keeping a wound clean and bandaged has been part of human history for a long time. Already as early as 2110 BCE, three healing gestures, named on a Sumerian clay tablet, were suggested: washing the wound with beer and hot water, making plasters (based on herbs, ointments and oils) and putting a bandage on the wound. Although various traditional medicine systems, such as Ayurveda, Chinese, Kampo and various European plant-based treatments, were recommended for wound cleansing and closures, probably the major breakthrough came with Dr. Lister who, in 1865, proposed the use of antiseptic in wound treatment, firstly as a wound dressing soaked in carbolic acid. The Johnson and Johnson company was, in 1891, the first to mass produce sterile surgical dressings. Fine mesh gauze, minimally adherent to wound surfaces and having limited absorption properties, was introduced in 1944. The first non-adherent bandage, Tefla, came onto market in 1954 (Broughton et al., 2006).

Where Are We Today?

In general, the consensus among scientists working on wound therapy state that the ideal wound dressing, including burn dressings, should achieve rapid healing at reasonable cost and with minimal inconvenience to the patient (Boateng, et al., 2008). Desired features of an optimal wound dressing or wound covering should include the ability to perform or mimic numerous actions of human skin such as not being permeable to bacteria and being adhesive, occlusive, lasting and elastic enough for patient not to feel discomfort (Alsarra, 2009). Managing moisture in the wound is a particularly challenging aspect in wound dressing development. The optimal dressing should be able to draw away components of wound fluid by providing good fluid-handling capacity while, at the same time, maintaining a moist environment. Fluid-handling capacity is, nowadays, essential feature of dressings (Harding et al., 2007). Modern wound dressings are often classified as modern precisely due to their ability to retain and create a moist environment around the wound to facilitate wound healing, unlike conventional wound dressings which did not posses these features (Boateng et al., 2008).

New generations of medicated dressings incorporate various active ingredients which possess therapeutic values such as antimicrobials, growth factors, and various supplements (vitamin C for example). The most advanced dressings include systems able to provide a controlled delivery of active substances at wound site (Boateng et al., 2008).

Burn care, in particular, has become much more proactive in past several years, offering new approaches such as the use of temporary skin substitutes in partial thickness or second degree burns, relieving the pain and improving healing rate (Demling, 2008). For example, sustained release silver dressing provides antimicrobial treatment; reduction in patients' discomfort and in frequency of dressing change; and prevention of burn infection, one of the most common causes of impaired healing (Atiyeh et al., 2007).

NANOTECHNOLOGY AND NANOMEDICINE

Probably two of the most common key words in novel drug delivery system development, nanotechnology and nanomedicine offer great potentials in wound therapy, including burn therapy. The aim of this review is to summarize and comment on various types of formulations designed for burn therapy emerging for the fast developing field of nanomedicine. Most of the references cited in the chapter are related to burn therapy. However, some deal with different types of wounds rather than the burns, but the authors believe that they can be applied in burn therapy as well.

"Nanotechnology is concerned with materials and systems whose structures and components exhibit novel and significantly improved physical, chemical and biological properties, phenomena and processes due to their nanoscale size," is one of the most descriptive definition of nanotechnology given in 2000 by the US National Nanotechnology Initiative (Riehemann et al., 2009). Nanomedicine, on the other hand, can be simply defined as an application of nanotechnology to medicine. Its approach is based on attempting to either kill specific cells or repair them, one cell at a time, by using a biosensor to detect, for example, the time for needed drug release (Riehemann et al., 2009). Nanomedicine focuses on development of nanoparticles and nanostructured surfaces as well as specific nanoanalytical techniques. The progress in nanotechnology opens possibilities for targeting and successfully delivering drugs and various active agents, resulting in improved drug efficiency, improved patient safety and compliance, with simultaneous reduction in side effects (Murday et al., 2009).

NANOMATERIALS

Nanomaterials, often referred to as nanobiomaterials as their targets are biological applications, are materials composed of synthetic or biologically derived moieties which can be successfully applied in diagnostics or therapy, irrespective of their origin (Singh et al., 2010). In an extensive review on those nanomaterials with a potential in wound therapy, Singh et al. (2010) summarized the advantages of nanoscale materials in wound management as:

- Providing the size and shape versatility of materials
- Having the ability to be applied with supported antimicrobials and filling materials, providing both mechanical advantages and therapeutic action

- Ability to make thin films in tissue repair, resulting in high surface area to volume ratio, diameter and pore size corresponding to natural tissue fibers, improved cell adherence, and controlled degradation rates *in vivo*
- In addition, mechanical strength and light weight, preventing the compression of wounded area.

Nanomaterials have proven potentials in wound therapy. The form in which they will be applied onto the wounded area depends on the type of material and aim of the therapy. For example, as an example of nanomaterials used for improved wound therapy, Shukla et al. (2010) developed a layer-by-layer assembly of polymer thin films bearing peptide antimicrobial agents. The films provided control over drug release kinetics (release up to 10 days), and were found to be biocompatible with the wound, offering local delivery of new therapeutic agents and preventing the development of bacterial resistance.

Nanofibers as Wound Dressings

Nanofibers, mimicking collagen fibrils in the extracellular matrix, can be manufactured from a host of natural and synthetic compounds to exhibit the properties that are beneficial for burn care (Hromadka et al., 2008). The large surface area is particularly suitable to provide sustained release of various antimicrobial agents, analgesics, or growth factors. Their high porosity enables the diffusion of nutrients and waste. Controlled degradation rates promote the scaffold absorption after the function is no longer required (Burger et al., 2006).

Drug molecules incorporated into a polymer matrix can be present in three states, namely dissolved in the nanofiber; in the form of particles; or embedded as a core, encapsulated by a shell polymer (Hromadka, et al. 2008). The release of the incorporated drug can then be controlled by the characteristics of nanofibers, particularly their porosity.

A nanofibrous polyurethane membrane developed by Khil et al. (2003) showed superiority in exudating the fluid from the wound, and, at the same time, maintaining the moist wound environment. Moreover, it showed controlled evaporative water loss, excellent oxygen permeability and inhibition of microorganism invasion. Chitin and chitosan can also serve as polymers for electrospinning and developing superior nanofibers to be applied to wounds (Min et al., 2004).

Rho et al. (2006) developed cross-linked collagen nanofibers coated with extracellular matrix proteins that were very effective as wound-healing accelerators in the early-stage of wound healing.

Coaxial electrospun thermoplastic polyurethane/collagen compound nanofibers for tissue engineering applications, an interesting approach to the development of functional biomaterials with potentials in wound therapy, were proposed by Chen and co-workers (2010). The biomimetic nanofibers were developed to serve as biomedical scaffolds.

Nanofibers as polymer matrices are especially interesting for drugs that are currently applied onto wounds in solution form, as well as for tissue engineered skin. Nanofibers have the ability to mimic the extracellular architecture and can, therefore, serve as a temporary extracellular matrix until the natural tissue regeneration replaces the scaffold (Hromadka et al., 2008). They provide a 3-D environment with adequate porosity for cell proliferation and migration, easy diffusion of compounds to further modulate cellular functions and guide the

growing cells to self-organize into complex tissue. Nanofibers are expected to provide an almost unlimited supply of durable tissue engineered skin, in particular for larger burn wounds (Hromadka et al., 2008). Highly crystalline chitin nanofibrils formulated with chitosan glycolate and chlorohexidine were manufactured in three conventional dosage forms, namely spray, gel and gauze (Muzzarelli et al., 2007). A clinical evaluation confirmed their potentials. Moreover, the spray was recommended as a first-aid tool, the gel for areas with thin epidermal layers, and the gauze was found to be superior in respect to scarless healing.

Nanofiber-Based Cell Scaffolds

The approaches of culturing different live human tissues outside the body and subsequently applying them as cultured skin, relies on advanced nanofiber-based cell scaffolds. Various materials can be used to manufacture suitable nanofibers, such as alginate, for example (Singh et al., 2010). Very promising findings were reported by Schneider et al. (2009) who developed silk mats, made of electrospun nanoscale silk fibers containing the epidermal growth factor and providing the controlled release of the factors.

A bio-functionalized peptide scaffold exhibits slow and localized release of growth factors, stimulating the cellular proliferation and promoting angiogenesis to regulate the synthesis and degradation of the extracellular matrix (Singh et al., 2010).

Perhaps the biggest advantage of these systems lies in an opportunity provided by them to change/adjust the formulation, depending on the specific requirements of a particular patient (Yeo et al., 2008). Carbon nanotubes-based sheets and yarn can also be applied for this strategy, particularly for wounds with a composite need of different types of cells, such as burns (Galvan-Garcia et al., 2007).

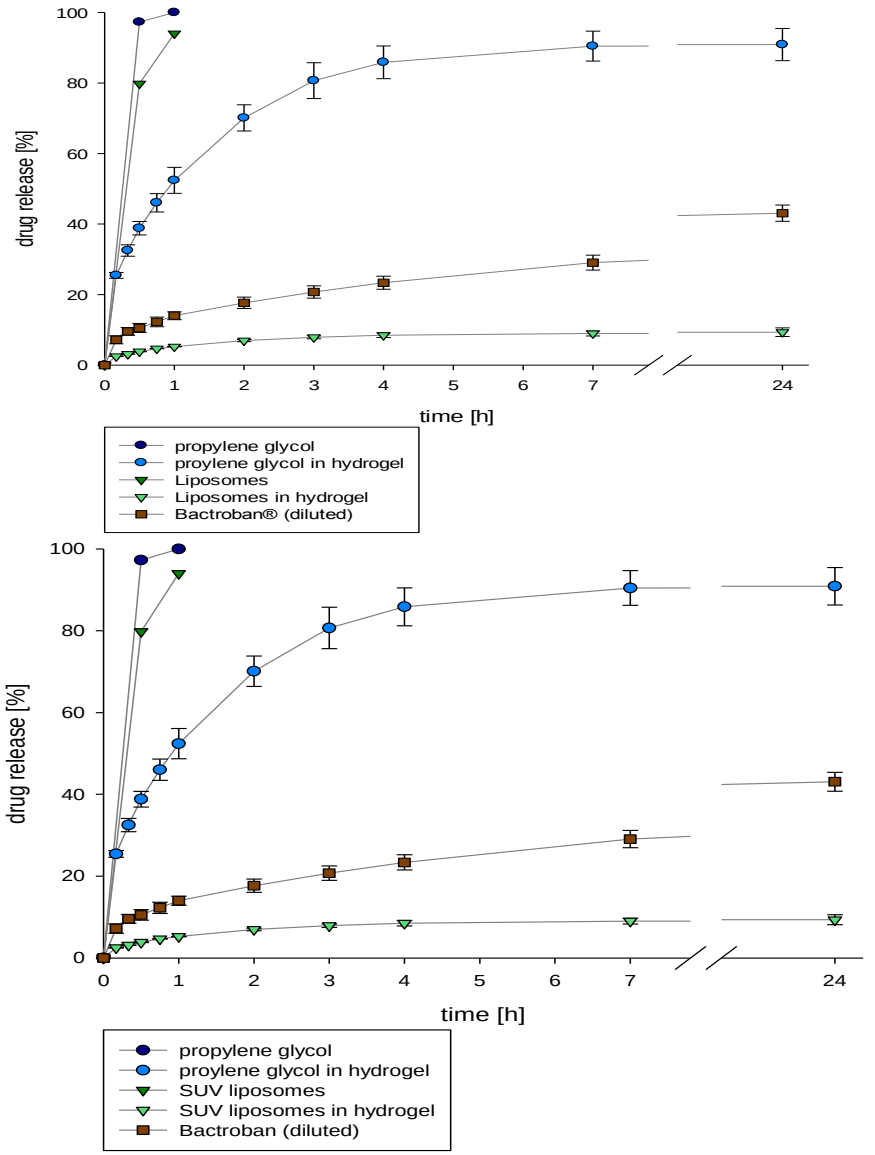
Polymer-Based Nanotherapeutics

Due to their specific features, such as versatile molecular structure, polymers are particularly attractive in tissue repair (Singh et al., 2010). By packing the functional moieties with drug conjugates, it is possible to design and have a certain degree of control over their surface properties. Particularly interesting is to include antimicrobial agents to prevent wound infections. The developments in nanotechnology, resulting in the control over desired physical properties (hydrophilicity, for example) and mechanical properties, particularly plasticity, brought the potentials of polymer-based nanomedicine to a higher level (Vicent et al., 2008).

Nanomaterials for Autologous Skin Grafts and Skin Equivalents

Engineered living skin was initially developed to treat burns when autologous grafts were unavailable (Eisenbud et al., 2004). Bioadhesive substrates for engineering the cell matrix assembly for autologous skin grafts seem to be another promising application of nanomaterials (Geckil et al., 2010). This approach provides an opportunity to prepare autologous skin grafts from a patient's own skin. Peng et al. (2008) prepared a composite

nano-TiO2-chitosan with collagen artificial skin (NTCAS) and with a time-dependent rate of biodegradability, moderate water absorptivity, low density and a very fine thickness, ideal characteristics of artificial skin equivalents. Moreover, it showed a uniquely potent bactericidal property. According to the authors, it was found to be superior to any currently marketed product.



Mupirocin was: 1) dissolved in propylene glycol, and either tested as solution (dark blue circle) or as incorporated in hydrogels (light blue circle), 2) incorporated in small unilamellar vesicles (SUV, dark green triangle) or in SUV incorporated in chitosan hydrogels (light green triangle), 3) in Bactroban® cream, diluted to a concentration corresponding to the concentration in liposomes and propylene glycol (brown square).

Figure 1. Mupirocin release profile (cumulative) from various formulations (n=3).

NANOPARTICULATE DRUG DELIVERY SYSTEMS IN WOUND TEHRAPY

Particles in the nano size range have very specific properties with promising potentials to allow for the targeted delivery of a drug (Petros and DeSimone, 2010). The rational design of such nanoparticles could enable their broader utilization, leading to clinical application as an ultimate goal. It is rather hard to classify different classes of nanoparticles, and we tried to classify them based on the material used in their manufacturing or the destined treatment. Some of the particles are overlapping between the categories, such as silver- based nanoparticles that are destined for antimicrobial therapy, but are made of a specific material and are, therefore, separated.

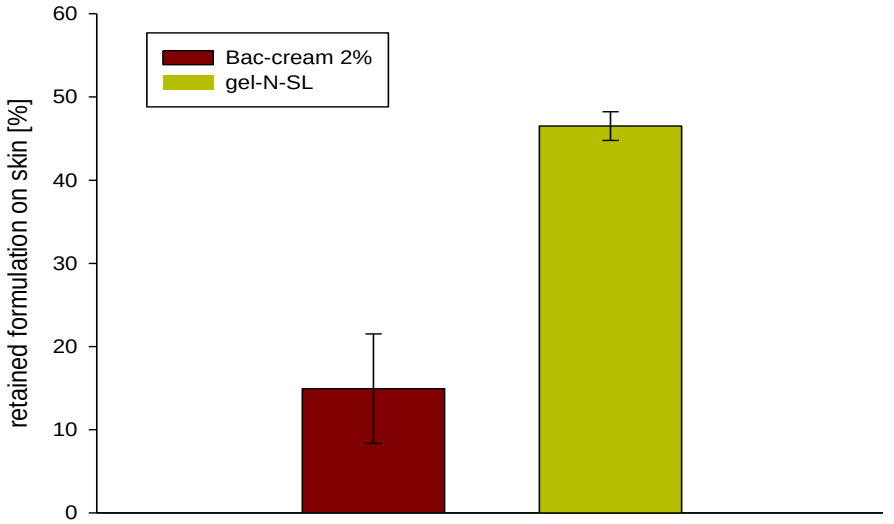
Nanoparticles as Carriers for Antimicrobials

Burns are characterized by their disrupted skin barrier properties, as well as many systemic host defense mechanisms, making skin susceptible to microbial colonization, and leading to burn wound sepsis if untreated (Cortivo et al., 2010). Delivery of antibiotics via nanoparticulate carriers can provide the possibility for the controlled release of antibiotics over longer period of time. Several different antimicrobials were tested as proof of this concept (Cortivo et al., 2010). We have been interested in liposomally encapsulated mupirocin, an antibiotic with strong activity against *S. aureus*, one of the most common human pathogens. Liposomes, however, have a tendency to be removed from the topical administration site due to their liquid nature (Pavelic at al., 2001). In order to assure that liposomes remain over longer period of times at the wounded site, we prepared liposomal hydrogels and obtained the sustained release of mupirocin over a longer period of time (Hurler et al., 2011; Figure 1)

A very important feature of any delivery system to be applied onto the wound is their ability to stay at the wound site and assure prolonged contact between the incorporated drug and the wound. In our laboratory, we are developing liposomal hydrogels, made of chitosan, that have shown increased bioadhesion in comparison to conventional dosage forms such as creams (Figure 2).

Nanocrystalline Silver and Silver-Based Nanoparticles

Whereas antimicrobial properties of silver have been known and used for many centuries, silver in burn wound treatment had disappeared around the Second World War, and it took many years until its rediscovery. Today silver ions in form of silver nitrate or silver sulfadiazine are frequently used in burn wound care. Newer products use nanocrystalline silver, e.g Acticoat^{TM}, instead of the ionic form. Silver ions are highly reactive and bind to negatively charged proteins, RNA, DNA and others and is thereby among others inhibiting DNA replication, which is the main mechanism of its antimicrobial effect (Atiyeh et el., 2007). Acticoat^{TM} consists of two outer layers of high-density polyethylene net, coated with silver and provide an antimicrobial property, and one layer of rayon/polyester gauze in between, keeping the wound moist (Khundkar et al., 2010).



The bioadhesiveness was determined on the porcine ear skin by the help of Texture Analyzer (TA.XT. Plus Texture Analyser, Stable Microsystems, Surrey UK).

Figure 2. Bioadhesiveness of newly developed liposomal hydrogel for mupirocin (gel-N-SL) in comparison to conventional mupirocin cream (n=5).

Acticoat™ improved the bacterial clearance compared to other silver-containing dressings. Due to its sustained release of silver, Acticoat™ requires less frequent dressing changes than conventional wound dressings do. In comparison to wound care with chlorhexidine acetate 0.5% and silver sulfadiazine in full-thickness burns contaminated with *Acinetobacter baumanii*, in Wistar rats, Acticoat™ was shown to be superior. It prevented penetration and the systemic spreading of *A. baumanii* in all tissues more efficiently than the other dressings (Uygur et al., 2009). Acticoat™ was also proposed as the treatment of choice for *Candida albicans*-contaminated full-thickness burns in Wistar rats, in comparison to chlorhexidine acetate 0.5% and nystatin. In regards to the broad spectrum of antimicrobial activity and less frequent dressing changes, Acticoat™ was found to be superior to conventional treatments (Acar et al., 2011).

Nanocrystalline silver can be also combined with natural polymers. Lu et al. (2008) compared the healing rate of silver-coated chitosan films, silver sulfadiazine and chitosan film in deep partial-thickness wounds in Spague-Dawley rats. The silver nanocrystalline chitosan dressing showed significantly shorter healing time than the control groups. In addition, the silver concentration in blood and tissues of rats treated with the silver chitosan dressing was lower than in animals treated with silver sulfadiazine. A similar effect was shown by Huang et al. (2011): the treatment with chitosan, coated with nanocrystalline silver, increased the survival rates of mice with full-thickness burns infected with *P. aeroginosa*, compared to chitosan alone at significant level. A comparative *in vitro* study showed that silver has good antimicrobial properties; however, the potential toxic effects should be monitored. Whereas nanocrystalline silver and ionic silver showed no difference in antimicrobial properties and antioxidant capacity, nanocrystalline silver featured better cell viability and proliferation than ionic silver when embedded in alginate (Wiegand et al., 2009).

In addition to antimicrobial properties, silver has been shown to promote wound healing through the reduction of cytokine-modulated inflammation, thus promoting scarless wound healing (Tian et al., 2007).

Nanoparticles as Carriers for Nitric Oxide (NO)

Nitric oxide possesses a broad spectrum of antibacterial properties against both Gram-positive and Gram-negative bacteria, and several different small molecules were proposed as a carrier able to increase its delivery in the wounded area (Cortivo et al., 2010). An interesting approach was proposed by Hetrick et al. (2009) by using silica nanoparticles as a NO carrier, resulting in enhanced bactericidal efficiency. As observed earlier for silver oxide therapy, NO-silica nanoparticles were also reported to exhibit the inflammation-modulating properties, as well as tissue remodeling abilities, and have great potentials in improved wound therapy (Cortivo et al., 2010).

Liposomes in Burn Therapy

Liposomes are the most clinically established nanometerscale systems for drug delivery. Their excellent biocompatibility, biodegradability and possibility to manipulate their size and surface properties, makes them an ideal nanovector in drug delivery (Riehemann et al., 2009). Their strongest potentials are in non-viral gene therapy for wound healing, discussed in the section on gene therapy. A very promising approach was proposed by Vogt et al. (2006) by using PVP-iodine in hydrosomes, a specific type of lipsoomes, in hydrogels for reduced loss of skin grafts.

Solid Lipid Nanoparticles and Dendrimers

Similarly to liposomes, solid lipid nanoparticles also offer excellent biodegradability and biocompatibility. Wolf et al. (2009) prepared solid lipid nanoparticles and dendritic coremultishell nanotrasporters embedded with several opioids and achieved increased cell migration and closure of experimental wounds in a concentration-dependent manner. They attributed the effect to the specific receptor interaction. The effect was found to be chemotactic, rather than chemokinetic. Therefore, opiods loaded into solid lipid nanoparticles can serve a dual purpose, namely as both pain reducing agents and healing enhancing systems.

Nanoemulsions

Nanoemulsions are composed of water, surfactants for stabilization and an oily phase and are characterized by a droplet size in nanoscale (Zhou et al., 2010). They have several desirable properties such as controllable droplet size, relatively long-term stability or powerful solubilisation ability. Nanoemulsions are employed in various routes of

administration, such as intravenously, orally or ocularly. Although they might have advantages in regard to low skin irritation and high loading capacities, nanoemulsions are, up to now, rarely studied for skin application (Mou et al. 2008).

Hemmila et al. (2010) could show promising effects on the improved wound healing of partial-thickness burns in rats treated with nanoemulsion. Bacterial growth in infected wounds (*P. aeruginosa*) was reduced and their inflammatory response was found to be decreased (Hemmila et al. 2010). Greenhalgh and Turos (2009) developed polyacrylate nanoparticle emulsions for enhanced wound healing, shortening the healing time in a murine model.

NON-VIRAL SKIN GENE THERAPY

Gene therapy is defined as the insertion of a gene into recipient cells (Branski et al., 2009). The skin is a very attractive organ for gene therapy, especially since targeted sites such as fibroblasts and keratinocytes are rather easy to harvest and cultivate, providing an opportunity to use skin cells as vehicle in gene transfer (Khavari et al., 2002). An additional advantage is the fact that skin is an easily accessible organ and the therapy outcome of skin treatment can be easily monitored. In general, in order to introduce and express foreign DNA into host cells, two basic approaches have been suggested:

a) gene therapy, relying on permanent insertion of DNA, and
b) gene medicine, used for transient transformation and short-term expression of a gene product (Khavari et al., 2002).

Burns are characterized by high cell activity and high proliferation rates, necessary for efficient dermal gene transfer (Felgner et al., 1995).

Moreover, the approaches can be also classified as *in vivo* techniques, in which genes are directly introduced into the target tissue and *ex vivo* techniques, based on isolation and cultivation of selected cells with *in vitro* transfection, followed by the subsequent transplantation to host. In both approaches, the selection of the vector for genetic material is determining the success of treatment (Branski et al., 2009).

The three "R"s concept in burn therapy (replacing, reconstructing and regenerating) has been transformed into transplantation, tissue engineering and, recently, stem cell therapy (Burd et al., 2007). Although the concept of skin replacement was proposed as the ultimate solution in wound and burn therapy, skin tissue engineering in praxis resulted in skin substitutes aiding in wound healing and repair, temporary skin replacement and aiding to regeneration (Burd et al., 2007).

To accelerate wound closure, genes encoded for growth factors or cytokines showed very strong potentials (Branski et al., 2009).

Viral vectors are not the focus of this article and are, therefore, not reviewed here. However, for an extensive overview on viral vectors in skin gene therapy, the readers are referred to Branski et al. (2009).

In order to avoid possible antigenicity of viral vectors, non-viral methods have been developed that are able to deliver genes to target cells without the inherent disadvantages such

as antigenicity, potential for recombination with wild type viruses and possible damage as a consequence of repeated exposure to viruses (Davidson, et al., 2000).

Non-viral gene therapy has several advantages over viral gene therapy as the delivery systems used for this purpose are rather easy to manufacture, simple in structure, direct in application, and cost-effective without the requirement for *ex-vivo* manipulation (Jeschke et al., 2001). The main advantage is definitely their safety, in contrast to viral delivery systems.

Non-viral methods used in gene delivery can be broadly classified as:

Chemical: liposomes, nanoparticles, calcium phosphate precipitation, DEAE-dextran and polybrene/DMSO

Physical: irradiation, microinjection, microseeding, muscle injection, electroporation, biolistic/particle-mediated bombardment (Davidson et al., 2003)

Several approaches in non-viral gene delivery have been proposed:

i) Naked cDNA, in the early nineties, Hennge et al. (1995) injected naked genes into the skin and determined a significant recruitment of dermal neutrophiles. In spite of the promising approach, the transfection efficiency was found to be low, and the level of the initial degradation to be high prior to the injectate reaching the cytosol. Naked DNA constructs exhibit fragility in the extracellular environment, are rather large in size and possess electrical charge, preventing successful penetration into the cells (Vogel, 2000).

ii) Micro-seeding technique delivers by the help of micro-needles putting naked DNA directly into the cell. The method was proposed by Eriksson and co-workers (1998) by using solid needles mounted on a modified tattooing machine. They succeeded to maintain elevated levels of transferred DNA for one or two weeks. However, transfection was only observed in the superficial layers of skin without reaching deeper tissue.

iii) Gene gun or biolistic transfer or the propulsion of micron-sized gold particles coated with DNA into the cytoplasm of cells using high-pressure helium as propellent. The efficiency of this approach was directly linked to the amount of stratum corneum left on the dermis (Davidson et al., 1999). The gene gun represents an approach based on micron-sized gold particles or tungsten-coated particles carrying DNA plasmids propelled into the skin (Davidson et al., 2003). The highest expression can be reached between the first and the third day of injection (Eming et al., 1999). Bombardment with growth factors or their receptors is one of the more promising approaches. The advantages include ease and speed of preparation of the delivery vehicle, the stability of the DNA preparation, absence of viral antigens, targeting potentials and rapid shedding of both particles and DNA if they are targeted to the epidermis. Still, the clinical applications remain not to be fully utilized, as the efficiency, potential tissue damage due to particles impacts, and coverage area remain to be challenges (Davidson, et al., 2000). Nanney et al. (2000) proved in *in vivo* experiments on porcine partial-thickness wounds that gene gun delivery systems can boost epidermal growth factor expressions; however, the issue of the depth reached by this approached remained questionable. Improvement in gene gun delivery systems based on higher discharge speeds resulted in higher levels in gene expression in both epidermis and dermis, as showed by Dileo et al. (2003).

Electroporation was proposed as method to improve the healing of chronic wounds. Lee et al. (2004) reported a synergistic use of electroporation, where an electric field was applied to tissue, in combination with tissue growth factor-β1 cDNA, in a diabetic mouse model. Although electroporation and the simultaneous administration of keratinocytes growth factor (KGF) plasmid DNA increased wound healing, no significant improvements in comparison to the treatment without electroporation were seen (Marti et al., 2004). The effect of electroporation remains to be questionable.

iv) Biomatrices: polymer based matrices, such as proposed by Megeed et al. (2002a). Polymeric matrix-controlled gene delivery systems provide many advantages over the bolus approach, common in gene therapy. Particularly interesting are:
   a) ability to manipulate and control the DNA release profile, achieving sustained and predictable delivery, improving the therapeutic efficiency
   b) ability to localize delivery to a specific site (injection or implantation)
   c) provide protection to DNA against endogenous nucleases (due to the polymer matrix) (Megeed et al., 2002b).

The authors suggested that genetically engineered silk-elastinlike polymers (SELPs; combination between silk-like and elastin-like blocks) may serve all the above mentioned purposes.

v) Liposomes

Liposomes offer potentials in varying lipid compositions and vesicle sizes to improve intracellular delivery (Peschka-Suss and Skalko-Basnet, 2000). For an extensive review on liposomes as a non-viral gene delivery system, the readers should refer to Jeschke et al. (2001).

Enhancement of dermal and epidermal regeneration represents a crucial target for the treatment of wounds, including burns. Although growth factors were proposed as one of the promising approaches, their clinical application remains to be rather limited. New strategies were proposed based on gene therapy (Jeschke et al., 2001).

A very important aspect for the growth factor wound-healing paradigm is the effective delivery of these polypetides to the wound site. As a site, a wound is a very hostile environment (Davidson et al., 1999). A carrier molecule, able to serve as both protector and delivery system for growth factors, is a prerequisite for their successful application in wound therapy.

By inserting a gene into the cells involved in the wound healing process, it should be possible to engineer the synthesis and delivery of a specific therapeutic protein into the wound site using a permanent or transient gene expression system.

Jeschke et al. (2000) studied mechanisms, transfection rates and the biodistribution of liposomal gene transfers in the skin of thermally injured rats using cDNA gene constructs coding for insulin-like growth factor-I and Lac Z gene for β-galactosidase. The studies were conducted in rats with a full-thickness scald burn. The translated IGF-I protein was found biologically active in the skin by increasing skin cell proliferation and accelerating re-epithelization 33 days after the thermal injury. Importantly, no systemic transfection was

detected. Cholesterol containing cationic liposomes, encapsulating an expression plasmid vector for cDNA, was proven to be able to deliver biologically active proteins to the skin.

The keratinocyte growth factor (KGF) stimulates epithelial cell differentiation and proliferation, major steps in successful wound healing. Liposomal cDNA gene complex was proposed as a delivery system for KGF therapy. Clear improvements in epidermal and dermal regeneration were seen in rats with acute wounds (Jeschke et al., 2002).

In order to avoid the need for repeated injections of cationic liposome-cDNA complexes over time necessary for wound to heal, Bhattacharyya et al. (2009) proposed a single subcutaneous administration of an electrostatic complex of platelet derived growth factor B (rhPDGF-B) plasmid, integrin receptor selective RGDK-lipopeptide 1 and cholesterol, capable of healing wounds in model chronic wounds.

STEM CELLS IN WOUND THERAPY

Transient gene therapy provides means to improve wound healing, as a transient increase in strategic growth factors is required until the wound closure is complete. Embryonic and adult stem cells, with their prolonged self-renewal capacity and ability to differentiate into various tissues, are one of the lines within improved wound therapy (Branski et al., 2009).

Due to complexity of the wound healing process, creating a viable skin substitute though assembling individual components *in vitro* remains to be solved (Burd et al., 2007; Branski et al., 2009). It is evident that the plasticity of the different types of stem cells, both *in vitro* and *in vivo*, promises clinical applicability in the near future, as long as certain levels of control over their particular differentiation pathways are maintained (Branski et al., 2009). Burns are a particularly interesting target in stem cell research, as the prospect of possible replacement of damaged tissue by the regeneration process has a great impact on the wound healing (Burd et al., 2007).

Burd et al. (2007) reported on an application of analogous bone marrow to a chronic unhealed burn wound, causing the change into re-epitelializing wound able to become closed by graft. Similarly, Rasulov et al. (2005) applied allogenic bone marrow mesenchymal stem cells in the treatment of deep skin burns in patients.

BIORESPONSIVE NANOMEDICINE FOR WOUND REPAIR

Polymeric materials that respond to a stimulus are often called “smart” or “intelligent” due to their intrinsic ability to alter their physical and/or chemical properties and are one of the most promising lines in nanomedical research (You et al., 2010). Moreover, many of the polymers have the ability to rapidly respond to the environmental changes but are also able to return in the original state. The response to stimuli can be seen through different forms such as individual chain dimension/size, shape, surface characteristics, solubility, etc. (You et al., 2010).

In conventional drug delivery, an entrapped molecule is slowly released by either diffusion or upon degradation of the network. As a consequence, a typically early peak in drug concentration is achieved, followed by steady, linear release. In respect to topical

therapy, the drug might be present in too low concentrations to be effective, or too high concentrations resulting in toxicity. A drug carrier able to respond to external stimuli provides greater control over temporal and spatial drug delivery. By tuning the formulation or chemical properties of a polymer, the sensitivity to stimuli can be precisely controlled (You et al., 2010). Nanotechnology offers almost unlimited potentials in optimizing the bioresponsive materials.

The main concept of bioresponsive drug delivery relies on three basic components, namely the biosensor (able to detect external signals), signal processing (determining when to respond) and the actuator (providing drug release). In addition, the system should protect the drug and assure controlled release (Park, 2008). Below, we have selected several of the most representative examples of potentials of bioresponisive materials in burn and wound therapy.

Bioresponsive hydrogels (Ulijn et al., 2007) are "smart" biomaterials able to change properties in response to selective biological recognition events. When exposed to various biological targets (receptor, antibody, enzyme, nutrient, etc.), molecular recognition events trigger changes in molecular interactions that are translated into macroscopic responses (swelling/collapse or solution-gelling transition). Bioresponsive hydrogels offer great potentials in skin regeneration and/or wound healing (Park, 2008).

The advantages of hydrogels, including bioresponsive hydrogels are in their ability to provide a semi-wet, three-dimensional environment (due to inert surfaces), provide the possibility of a covalent linkage for incorporated biological molecules, their mechanical properties can be manipulated and they can be responsive to various triggers, and many hydrogels are antifouling(Park, 2008). Caldorera-Moore and Peppas (2009) summarized the potentials of nanotechnolgies as responsive biomaterial-based medical systems for various targets and purposes in drug delivery.

The fact that proteases play an important role in wound healing and cell differentiation, bioresponsive hydrogels that are able to respond to changes in protease concentration have a promising future in wound healing. The ultimate goal is the development of bioresponsive materials able to direct cell behavior in wound healing (Park, 2008).

Hardwicke et al. (2008) proposed dextrin-rhEGF conjugates as bioresponsive delivery systems for wound repair. The concept they applied was Polymer-masking-Unmasking-Protein Therapy (PUMPT). The concept uses a biodegradable polymer to transiently mask a protein during transit (thus stabilizing/inactivating the protein) while subsequently allowing triggered polymer degradation, protein unmasking and protein bioactivity. Succinoylated dextrin and rhEGF were the first model combination. The complex exhibited increased stability towards proteolytic degradation by trypsin and neutrophil elastase. Dextrin provided sustained release of rhEGF (50% released after 7 days). The conjugate was developed in order to protect the growth factor from the harsh wound's fluid environment, allowing for the regeneration of activity with time when exposed to α-amylase in physiological concentrations.

The potential was further confirmed in models of chronic wounds. The ability of dextrin-rhEGF to release rhEGF in wound fluid was determined in *in vitro* settings (Hardwicke et al., 2010).

Biodegradable thermosensitive hydrogels, based on triblock copolymers, poly[ethylene glycol-b-(D, L-lactic acid-co-glycol acid)-b-ethylene glycol] (PEG-PLGA-PEG), as carrier for gene therapy in wound healing were proposed by Li et al. (2003).

Sodium salt of 2-acryloamido-2-methylpropanesulfonic acid (Na-AMPS) photopolymerised with ethylene glycol dimethacrylate (EGDM) as a cross linking agent and 4,4'-azo-bis(4-cyanopentanoic acid) as the water-soluble photoinitiator were shown to have potential as wound dressings. Photopolymerized Na-AMPS-based hydrogel was found to be non-toxic, exhibiting fast water absorption and appropriate balance of water vapor transmission (Witthayaprapakorn et al., 2008).

Potentials of PUMPT using hyaluronic acid (HA) conjugates to mask activity and enhance protein stability were evaluated by Ferguson et al. (2010). The authors showed potentials of HA conjugation in resisting degradation at sites of inflammation through enhancement in stability of HA-trypsin conjugates in the presence of elastase. Those could lead to a reduction in the frequency of administration as well as dose, resulting in better treatment.

Repeated administration of non-biodegradable polymers may be associated with vacuolization, lysosomal storage diseases and even pathological metabolic changes (Chi et al., 2006). Hyaluronic acid is a naturally occurring polysaccharide, with antimicrobial, wound healing and tissue regeneration properties. It is one of the most attractive substances with potentials for improved wound healing (Ferguson et al., 2010).

GROWTH FACTORS

Although some of the earlier mentioned delivery systems were designed as carrier systems for growth factors due to their potentials in improved wound therapy, growth factors are separately highlighted. Growth factors have been confirmed, in animal models, to enhance epidermal and dermal regeneration. However, in humans, their efficiency has not been confirmed. The failure can be attributed to high concentrations of proteases in wounds that rapidly destroy all proteins applied to the wounds. In addition, receptors available for the growth factors are decreased, reducing the initiation of the signaling cascade (Jeschke et al., 2002).

Although the concept of bringing growth factors (EPG) to wounds in order to promote wound healing is rather old clinical improvements in wound healing were limited due to premature inactivation of growth factors in wound environment until recently.

The biological activity of growth factors at the wound site is limited due to:

- Their short half-life
- Inactivation by wound proteases
- Adherence to extracellular matrix components
- Poor bioavailability from delivery carriers
- Need for high initial doses and frequent applications (Davidson, 2000).

Growth factors incorporated in various types of wound dressings resulted in various degrees of therapeutic efficiency (Alemdaroglu et al., 2006). Gelatin film dressing, incorporating epidermal EPG applied onto partial-thickness skin wounds in hairless dogs, showed improved wound healing (Tanaka et al., 2005). However, the aim of this review is to evaluate advanced systems, particularly nanoparticulate systems for improved wound healing.

Gene therapy offers promising potentials for growth factor or cytokine delivery to enhance wound healing. Acidic fibroblast growth factor (aFGF or FGF-1) is one of the most promising cytokines with applications in wound healing. Sun et al. (1997) proposed transfection with aFGF cDNA for improved wound healing. aFGF gene delivery resulted in both gene expression and a functional improvement in healing.

The limited success of growth factor therapy is attributed to limitations in their release profile, stability issues, rapid protein degradation or denaturation, and limitations of the carrier systems. Regranex®, a topically applied gel containing a recombinant human platelet-derived growth factor, became the first recombinant growth factor to be approved by US FDA to accelerate wound healing. However, its effectiveness remains to be rather limited (Steed, 2006).

Implementation of a polymer-based nanodrug delivery device bearing growth factors directly into the tissue can provide localized growth factor delivery. For that purpose, various biodegradable and non-biodegredable polymers have been evaluated. Most of the experiments up to now were aiming at the treatment of skin and gastric ulcers (Cortivo et al., 2010). Plasmid DNA encoding VEGF-165 activated collagen-chitosan dermal equivalents, developed recently by Guo et al. (2011), are an example of a sophisticated delivery system with a strong promise in treating full-thickness burn wounds.

ANIMAL AND ARTIFICIAL SKIN AS WOUND COVER

Besides traditional wound treatment there are also approaches to enhance wound healing by using biological dressings. For an extensive overview, the review by Rizzi et al. (2010) is recommended. In a prospective study, Hosseini et al. (2009) compared the healing process in second degree burn wounds that were treated with either lyophilized porcine skin (Xenoderm) or 1% silver sulfadiazine cream. Thereby, Xenoderm showed superior wound healing properties in regard to time of reepitheliazation, number of dressing changes and duration of hospital stay. In addition, the rate of wound infection was less for patients treated with Xenoderm (during hospital stay plus follow-up) compared to patients who received treatment with silver sulfadiazine cream (17.9% vs. 40.5%). The positive effects of the Xenoderm treatment were also reflected in decreased need of analgesics (Hosseini et al., 2009).

Whereas Xenoderm has at least a theoretical risk of zoonosis, Xe-Derma®, which is also derived from pig skin, prevents this problem by removing the epidermis and all other cells enzymatically from the skin. Afterwards, the residual matrix is dried and sterilized with radiation. A prospective study showed no significant differences in healing time and infection complications for second degree burn wounds in children for Xe-Derma® and a hydrogel dressing with high absorption capacity. Xe-Derma® showed pain relieving effects and no dressing changes were required, and it was shown to be superior over the synthetic temporary skin cover. In addition, it provided good wound monitoring possibilities due to its transparency (Zajicek et al., 2011).

Composite nano-titanium oxide-chitosan artificial skin (NTCAS) was shown to exhibit strong wound healing effects with both anti-inflammatory and bactericidal properties (Peng et al., 2008).

Recently, a 3D multilayer culture of human skin fibroblasts mimicking natural skin was proposed as a potential future skin graft for wound repair (Lee et al., 2009). In an elegant and extensive review, Lazic and Falanga (2010) summarized the bioengineered skin constructs and their potentials in wound healing.

MODELS FOR EVALUATION OF WOUND DRESSINGS

Over the years, many wound healing models have been developed and proposed as means to provide a deeper insight on the a) physiological processes during wound healing, which may lead to the improved therapy or b) the effectiveness of wound dressings and ways to improve activity of incorporated drugs. Each model has its specific advantages and limitations and, in our opinion, the choice of the model used in a particular experimental set-up will directly depend on the targeted information that the evaluators are expected to gain. Some of the models suitable for burn therapy are proposed in Table 1. We would like to refer to an excellent review on the advantages and limitations for various types of models published by Lebonvallet et al. (2010).

Rather straightforward models are the 2D models, providing defined conditions with good reproducibility that are, in addition, cheap and easy to use. However, those types of models are lacking the specific information a 3D model can provide and, even more importantly, the parameters which can be investigated in these simple type of models are very limited. 2D models can be also used to investigate wound infection and the effect/success of an antimicrobial treatment. Giannini et al. (2010) developed a wound model in which the interaction between the activity of antimicrobials, fibroblasts and wound biomaterials (e.g. alginate) could be studied in a reproducible manner.

Mono and co-cultures are very useful in investigating certain cellular level events occurring during the wound healing. Hayashi et al. (2009) proposed a perfusion endothelial cell culture model as suitable in evaluating the impact of plasminogen on the wound healing process. Plasminogen regulates the proliferation of endothelial cells by a temporal interaction and is hence an important factor in the process of wound healing.

Three-dimensional (3-D) models include more cell types than mono or co-cultures and show many intercellular interactions although innervations and vascular systems are missing in this type of model (Herman et al., 2009, Tokudome et al., 2010). 3-D models are easy to use; however, they are also more costly than 2D models. The consequence of having different cell types present is that they may exhibit variability, and the parameters in experimental set-ups are hard to control. Human skin explants, representing a special type of 3-D model, are even more diverse than pure cell cultures due to different surgical techniques applied in their preparation and the sample origin (sex, age, area of the body, etc). However, skin explants are closer to the *in vivo* conditions and can be used in various experiments and potentially standardized (Emanuelsson and Kratz, 1997; Kratz, 1998; Coolen et al., 2008; Lebonvallet et al., 2010**)**. In addition, they provide an opportunity to study the effects of environmental stress or aging of the skin, and are suitable to evaluate antimicrobial effects of wound dressings in wound infection (Steinstraesser et al., 2010).

However, before applying antimicrobial drugs and wound dressings *in vivo*, specific attention should be given to the potential toxic effects of the system. Antimicrobial potency

can be tested in infected skin models (both 2-D and 3-D models) (Steinstraesser et al., 2010; Giannini et al. 2010). In addition, interesting options are provided by the bacterial biofilms, used for testing antimicrobial potency and efficiency of antimicrobial-containing wound dressings (Lipp et al., 2010; Hill et al., 2010).

Table 1. An overview of available burn wound models

Model	Origin	Purpose of testing	References
membrane diffusion models		drug release (e.g. exudate dependent)	Steffansen and Herping (2008)
2-D models	mono-cellular	Insight on physiologic events during wound healing (e.g. inflammatory response, factors affecting healing, cellular response)	Hayashi et al. (2009)
	co-culture		Oberringer et al. (2007)
3-D models	human explant skin		Emmanuelsson and Kratz (1997); Coolen et al. (2008); Steinstraesser et al. (2010).
	human skin model		Schneider et al. (2009) Herman et al. (2009)
	infection (*S. aureus*)	infection	Steinstraesser et al. (2010)
		evaluation of antimicrobials	Giannini et al. (2010)
bacterial biofilms		testing effectiveness of employed antimicrobials/antimicrobial dressings	Hill et al. (2010); Lipp et al. (2010)
animal model	mouse	Improved wound healing	Gurung and Skalko-Basnet (2009)
	rat		Alsarra (2009)
	rabbit		Sezer et al. (2008)
	pig		Boucard et al. (2007)

When a new drug-containing wound dressing is in its early development stage, full attention needs to be given not only to its biocompatibility and effectiveness but also to the release behavior of the drug, which, in ideal cases, should be in a controllable manner. Steffansen and Herping (2008) designed a wound model for characterizing the release of ibuprofen from foam dressings. The foam is applied on different membranes with different pore sizes and with consequent variation in the access to an acceptor phase. Wounds with low and high exudate level are rather easily mimicked in this model, and the effect of wound exudate on drug release can be studied.

Besides *in vitro* models, a lot of different animal models are used in wound healing research. Animal models are connected with serious ethical concerns and are often limited in numbers of animals. Animal models integrate all parameters and display the nearest reality to testing in humans although several differences need to be taken into consideration. Animal experiments are expensive, time consuming and require very well trained researchers.

In Table 1, an informative overview of different wound healing models is proposed. The selected references should serve as starting points to the researcher when deciding on model selection.

CONCLUSION

It is evident that nanotechnology and nanomedicine offer almost unlimited potentials in wound, including burn, therapy. New potentials are appearing with each new technological discovery, and possible targets for therapy are being equally fast determined. However, several points need to be addressed in respect to the real applicability of nanotechnology and nanomedicine in clinical practice. Still, very little is known about a potential interaction between small particles (in nano range) and normal functioning of the cells, and data on toxicology and biocompatibility of nanoparticles. An establishment of international standards in evaluation remains to be addressed. Although several promising nano-based wound dressings are close to clinical applications, the safety issues need to be taken in consideration.

In conclusion, the future of nanomedicine in burn therapy is a promising one, but as with each new technology and pharmaceutical development, we need to take it with "cum grano salis".

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Chapter 3

POST-BURN HAND DEFORMITIES

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ABSTRACT

Optimal hand function is a crucial component of a high-quality survival after burn injury. This can be achieved only with a coordinated approach to the injuries.

Aim - To evaluate the clinical and functional outcomes of patients with burn's hand injury.

Methods - A retrospective review was carried out of the case notes of the patients. The case notes included the clinicians' notes and the nurses' entries during admissions in the Burns Unit at Selly Oak Hospital, University Hospital of Birmingham NHS Trust, outpatients clinics and correspondence with General Practitioners (Family Physicians).

Results - A total number of 22 patients were evaluated. 16 patients were children and 6 adults. The mean percentage of body surface burned was 10, 8 %. The most common type of burn was scalds. The mean interval between burn injuries and first release was 5, 3 years. Z-plasty was used in 8 cases, FTSG in 7, STSG in 12, W- plasty in 8. The ROM was full in 10 hands, good in 10 and fair in 3.

Conclusion - The findings suggest that with a multi-disciplinary team approach, proficient with the concepts and execution of appropriate treatment protocols, consistent results achieving maximum potential can be obtained for a patient with a burned upper limb.

LIST OF ABBREVIATIONS

AC:	Alternating current
AMA:	American Medical Association
DC:	Direct current
FT:	Full thickness
FTSG:	Full thickness skin graft
HF:	Hydrofluoric acid
JBCR:	Journal of Burn, Care and Rehabilitation

MPJ: Metacarpophalangeal joint
PG: Pressure garments
PIPJ: Proximal interphalangeal joint
PRS: Plastic and Reconstructive Surgery Journal
PT: Partial thickness
PTS: Patients
ROM: Range of motion
SJPRS: Scandinavian Journal of Plastic and Reconstructive Surgery
SG: Skin grafting
STSG: Partial thickness skin graft
TBSA: Total body surface area
TE: Tangential excision

INTRODUCTION

As more patients survive large burn injuries, attention has become increasingly focused on the functional outcome of those suffering thermal injury, rather than simply their survival. A crucial element of survival quality is the restoration of hand function [1].

The specific treatment of burns to the hand normally has no direct impact on survival; however, the functional outcome of such therapy largely determines whether or not the patient successfully reintegrates into society after burn centre discharge.

The reconstruction of the burned hand is one of the challenging problems in plastic surgery. An acceptable result depends on many factors, including initial tissue damage and depth of injury, immediate post burn care, definite operative management of the extremity, and postoperative physical therapy.

Reconstructive surgeons may have complete control of only the third of these factors. Emergency department physicians and general surgeons may provide the initial management of the injured patients who often have multiple surgical and medical problems at the time of presentation.

Hand care must be an intrinsic component of the burn care team. The most crucial factor for a good outcome of burn injury to the hand is the initial care. In most situations, the hand burn will have to be managed synchronously with the intensive care, wound care, skin coverage of the burns and issues of sepsis in a patient with an extensive burn.

The postoperative therapy relies heavily upon a well-trained physical therapist and a highly motivated patient and family. The reconstructive surgeon often sees the patient after severe contracture and deformity have occurred. Months to years may have passed between the time of the initial injury and the presentation. Function followed by form are the major goals in surgery of the burned hand.

Early wound closure and rehabilitation can facilitate restoration of hand function. Accordingly, the need for reconstruction can be minimised.

This review of our experience details a systematic approach to management of these complex injuries and the functional outcomes associated with this approach.

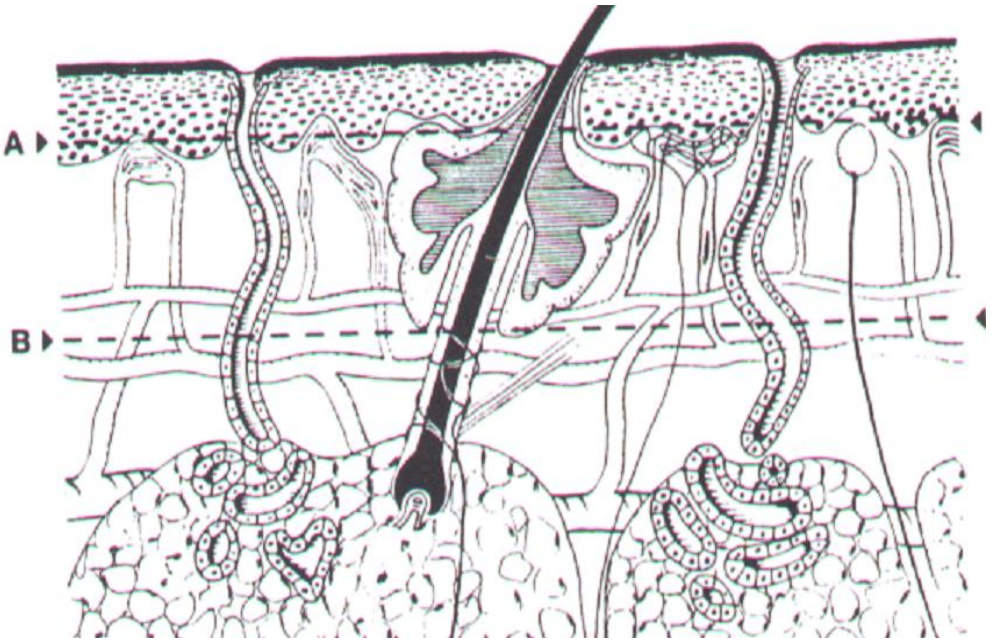


Illustration No: 1. Line A and B represent borderlines between dead and viable tissue in superficial and deep burns respectively [17].

Evaluation was according to the American Medical Association (AMA) impairment rating [2].

A. LITERATURE SURVEY

Types of Burns

The cause of the burn does make a crucial difference in evaluation and treatment of the hands. Thermal, chemical and electrical injuries are quite different and each must be understood.

Thermal Burns

Thermal injuries are by far the most common. A typical thermal hand burn involves the dorsum of the hand and may lead to a claw deformity.

The reason that thermal injury most uniformly produces this pattern is that the palmar skin is much thicker and therefore more resistant to full thickness injury (Illustration No: 1).

The temperature of the source has to be very high if deep burns are to be inflicted before the hand is withdrawn.

Also the hand is usually closed in a fist or used to cover the face or other body part during a burn. Therefore the dorsum is exposed and the palm is protected (Illustration No: 2).

Palmar lesions are much less common and occur in two unique circumstances:

(1) Adults with seizure disorders may grasp a hot object during a seizure or

(2) Children may grab hot objects such as irons or heating elements [2].

Children are prone to sustaining deep palmar burns because of a variety of anatomic and behavioural conditions. They are driven by curiosity, have a slower withdrawal reflex and possess a thicker palmar epidermis than adults.

Fortunately, a significant number of these injuries heal within a two-week observation period [1], [4]. When delayed healing occurs, however, hands can scar with flexion contractures of the fingers and a shortened thenar-hypothenar distance (Ill No: 3).

A priority in the treatment of hand burns is functional recovery of the injured hand. Good hand function improves the quality of life and allows for normal development of the child [5], [6].

Many surgeons consider early grafting as a means of expending recovery [7], [8], [9]. FTSG should be considered as a first choice for deep burns [10], [11].

Chemical Injuries

Many commonly used chemicals can produce burns. A chemical burn should be extensively irrigated similarly to thermal burn with consideration given to early excision if the injury is sufficiently deep [12].

Consultation with a toxicologist can help determine any chemical specific treatment or potential complications. The most commonly encountered chemicals which are treated so are described in Table No : 1.

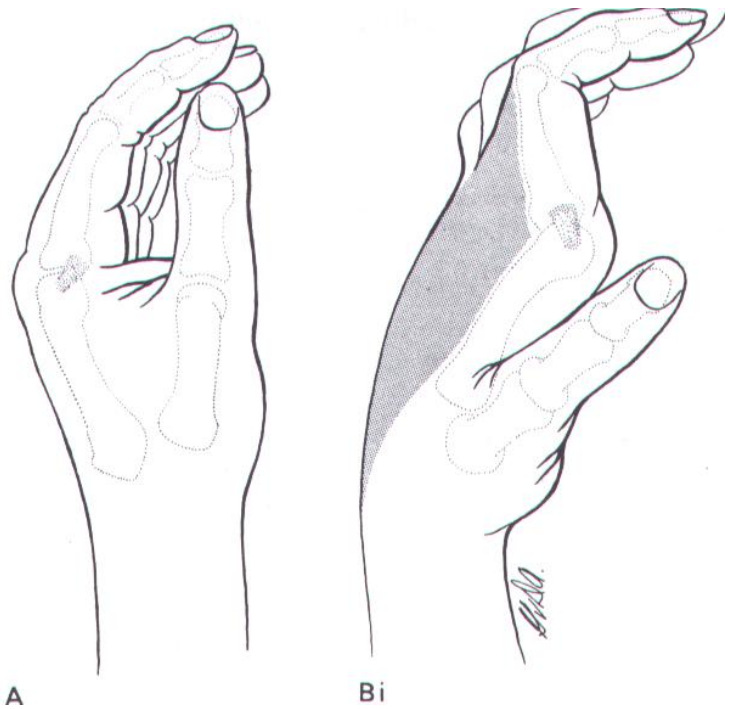


Illustration No: 2. A. Diagrammatic representation of the posture of the relaxed uninjured hand. B. With injury, oedema accumulates on the dorsal aspect of the hand. This drives the wrist into flexion, the MCPJ into hyperextension, the PIPJ into flexion and the thumb into adduction [12].

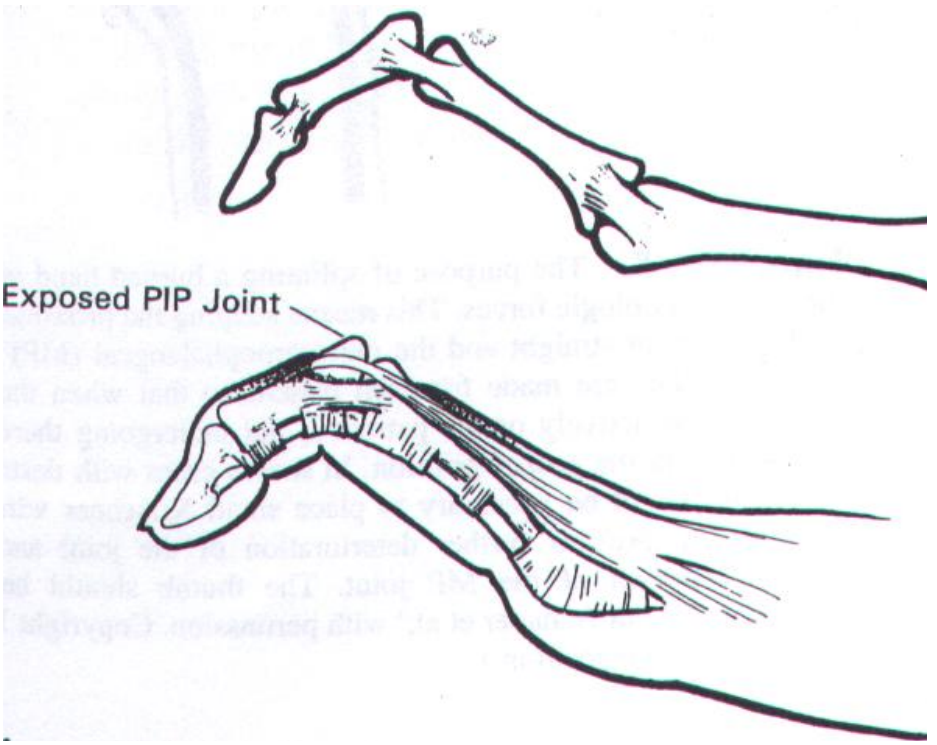


Illustration No: 3. Proximal interphalangeal (PIP) joint contractures. Deep burns over the dorsum of the PIPJ tend to destroy the extensor tendon mechanism. The strong flexor tendons cause a flexion deformity at this joint, which results in exposure of the joint [13].

Table 1. The most commonly encountered chemicals which are used so

Chemicals	
Alkyl mercuric agents	Gasoline hydrocarbons
Ammonia	Hydrochloric acid
Asphalt / tar	Lithium
Chromic acid	Lye
Cantharid	Nitric acid
Cement	Potassium emanate
Creosote	Propane
Dichromate salts	Sulphuric acid
Formic acid	Trichloracetic acid
Freon	

Five other common sources of chemical burn require most customised management:

- Hydrofluoric acid (HF)
- Phenol
- White phosphorus
- Elemental sodium and potassium (both explode on contact with water)

HF is widely used in industry for glass and metal cleaning and characterised by:

(1) deep, severe pain which may be delayed in onset.
(2) no apparent lesion at that stage.
(3) progressive skin necrosis, often subungal, progressing to bony erosion.

A HF burn is a very distinct problem. If untreated, the chemical will migrate to the distal phalanx and produce osteitis and a chronic wound that results in a painful finger tip, possibly requiring amputation [13].

Topical solutions of calcium or magnesium are helpful to neutralize HF. In addition, calcium gluconate can be injected into tissues to neutralize HF.

Alkali burns to the hand have some unique features that should be considered in management. Characteristically penetrate tissue more deeply and result in more tissue destruction than either acid or thermal burn in a given area.

Strongly alkaline solutions cause saponification of tissue lipids and react with these tissue lipids to form alkali soluble proteinates.

This reaction, itself destructive to tissues, is also exothermic and can generate sufficient heat to damage surrounding structures. The soluble alkaline proteinates that formed penetrate tissue further along with residual hydroxyl ions, which cause progressive tissue damage.

Unlike hypothermic injury, which ceases on removal of the heat source, this destruction proceeds until the alkali has been removed or diluted by body fluid.

In general, the severity and depth of cellular injury is proportional to the concentration of hydroxyl ion and the duration of exposure.

The alkaline-induced burn will generally result in full-thickness skin loss, usually destroying ectodermal elements in hair follicles and sweat glands.

This renders these wounds slow to heal.

The eschar of alkali burns, depleted of lipid component, results in greater evaporative water loss across it than across a thermal burn eshar.

Although malignancy can occur in any burn wound, Marjolin's ulcers seem to occur with a shorter latency period and perhaps more frequently after alkali burns.

The emphasis in treatment of alkali burns is to prevent ongoing tissue damage. Extensive copious irrigation with water for long period is the treatment of choice. Afterward, topical antibiotics and dressings are applied. Mafenide acetate (Sulfamylon) has the advantage of being both bacteriostatic and of combining with residual lye to form sodium acetate and mafenide radicals, both of which are thought to be innocuous to tissue [14].

-Electrical Burns

Most burns that occur from an electrical short are not actual conductive electrical burns; more commonly are flash burns. These burns are usually superficial and are treated the same as thermal burns [12].

True electrical conduction burns however are completely different and can be classified in two ways (Table No : 2). There is usually an entrance wound and an exit wound, which are generally fairly widely separated. There may be a small skin defect associated with massive damage to underlying muscles, nerves, or vessels.

Table 2. Classification of Electrical Injuries

Electrical Injuries	
1. - AC (alternating current)	(a) systemic effects : severe with ventricular fibrillation, respiratory arrest (b) local burn : often minor
- DC (direct current)	(a) systemic effects : moderate (b) local burn : severe
2. - LOW VOLTAGE ;i.e. :<1000V	(a) systemic effects : immediate if AC; none later (b) local burn : relatively minor full-thickness
- HIGH VOLTAGE ; i.e.;>1000V;often from high tension lines carrying up to 35000-averaging 14000V	(a) systemic effects : severe and sustained, including marked hypovolaemia, cardiac arrhythmias and renal failure (b) local burns : entry wound-full thickness exit wound – explosive arc burns, across joints thermal burns - clothing

Early decompression with fasciotomies and debridement is almost always required. Reconstruction can be long, complicated progress with modest results.

One can generalize that reconstruction following an electrical burn injury in a child is almost always indicated.

Children heal significantly better than adults, particularly as far as nerve grafts are concerned, and they can adapt well to anatomic changes.

A unilateral, major injury in adults, on the contrary, may best be treated by amputation of the hand. This may result in more rapid recovery and an excellent functional outcome with an appropriate prosthesis [13].

Severe bilateral injuries present a major problem. Usually an attempt is made to save the most severely injured hand or dominant hand if the injuries are similar in extent. Any available parts that may have later value in reconstruction should be salvaged if possible. Transfer of digits from hands that are unsalvageable to the other side (if digits are missing from the burn) may be a consideration.

However, it is a given that the patient will spend a long time undergoing reconstruction and rehabilitation. In any event the patient will have severe, significant disabilities.

Severe electrical burns need urgent decompression and fasciotomies on the day of injury (Illus. No : 4). Typically 2 -3 debridements are required to eliminate devitalised tissues. The eventual viability of underlying tissue may be difficult to evaluate and serial debridement may help this regard.

EARLY TREATMENT

There are four components to early treatment of burns:

(1) Evaluation of the depth of the injury
(2) Determination of the need for escharotomy
(3) Splinting
(4) Local wound care

Evaluation of the depth of the injury:

The treatment of all burns depends on an accurate diagnosis of the depth of the burn. The history of the accident is helpful. For example flash burns are superficial whereas electrical or molten metal injuries are deep and scalds cause intermediate damage [15]. It is notoriously difficult for even an experienced observer to estimate the acute depth of the initial burn accurately [13].

Numerous studies have been done to assess techniques of burn depth evaluation. The laser Doppler has been shown to be effective but is not usually available or applied clinically. It is used more as a research tool [16], [17], [18], [19], [20], [21], [22], [23], [24].

Fluorescein studies have not proved to be very useful. (If debridement is planned, depth can be determined by tangential shaving of the burned skin. When bleeding occurs, the tissue is considered viable.)

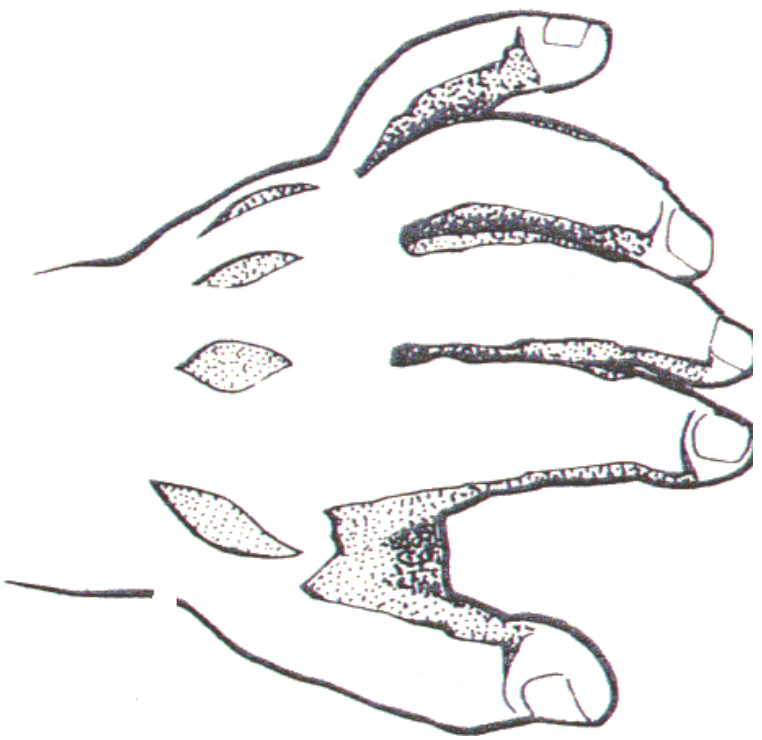


Illustration No: 4. Digital and intrinsic escharotomies. Escharotomy should be performed in areas that will not produce a contracture deformity after healing [13].

A superficial partial-thickness burn is red, painful, wet and shiny. Capillary blanching and return of colour occurs with local pressure and sensation to pin-prick is preserved. It will heal spontaneously in 10 to 14 days. At the other end of the scale there is usually no difficulty in diagnosing a full-thickness burn, whose dry surface eschar is hard and coagulated with a variable colour from pale white to carbonised black. Pain is not a major feature and the area is insensitive to pin-prick.

Healing is by slow marginal epithelial ingrowths. Between these extremes lie the deep partial-thickness or deep dermal burns which are frequently caused by scalds, have a pale pink or white surface, do not blanch and have reduced sensation to pin-prick.

Misdiagnosis is common even for the experienced. They will heal in 3 to 4 weeks from viable cells in deep skin adnexae if infection is controlled but cause significant scarring. These three depths of burn require different treatment.

Determination for the need of escharotomy:

Burned tissue is completely unyielding and can become a tourniquet if deep tissues are expanding, as is usually the case in burns. Vascular compromise may result, possibly leading to amputation [25].

Clinical signs associated with this problem include decreased capillary filling, decreased pulses, cyanosis and (the earliest sign) neurological changes.

Intrinsic muscle necrosis can occur in burned hand even in the case of detectable pulse.

Doppler measurements have been used to evaluate possible impending limb loss. A variety of techniques are available with which to perform the direct percutaneous measurement of tissue pressure. Basically, a fluid-filled needle contacted to a pressure monitor or transducer is inserted in to the deep tissues.

The pressure measured will slowly rise by passive equilibration to indicate tissue pressure. Effective tissue perfusion generally ceases at 40 mm tissue pressure, varying with systolic blood pressure and the degree of peripheral vasoconstriction. Such techniques have been advocated to indicate the proper time for surgical decompression. However, it has been practice, when serious problems are suspected, to perform immediate escharotomy or fasciotomy.

When circumferential burns of the hands and fingers are present, the escharotomies should be continued across the wrists and onto the fingers. Escharotomy should be performed on the thumb and on each involved finger (Illustration No: 4).

Splinting:

The hand must be positioned in an anticlaw position. The wrist should be extended to 35 degrees. The metacarpophalangeal joint should be placed in 40 to 70 degrees of flexion, the proximal interphalangeal joint in 10 degrees of flexion and the distal interphalangeal joint in 10 degrees of flexion. Additionally, the thumb should be maintained in the abducted position (Illustration No: 5).

In severe burns it may not be possible to place the hand in the anticlaw position with splints. Small Kirshner wires may be placed to fix these joints in extension. With these joints under control, metacarpophalangeal flexion is easy to obtain. This usually can be accomplished with a splint.

Splints are applied using rolled gauze or compressive wraps. A splint is fitted within 24 hrs for positioning of the extremity in the anticlaw position and is worn for 24 hrs a day except during exercise and bathing. Elevation of the injured hand above the heart for 2 to 3 days is useful to prevent oedema [26].

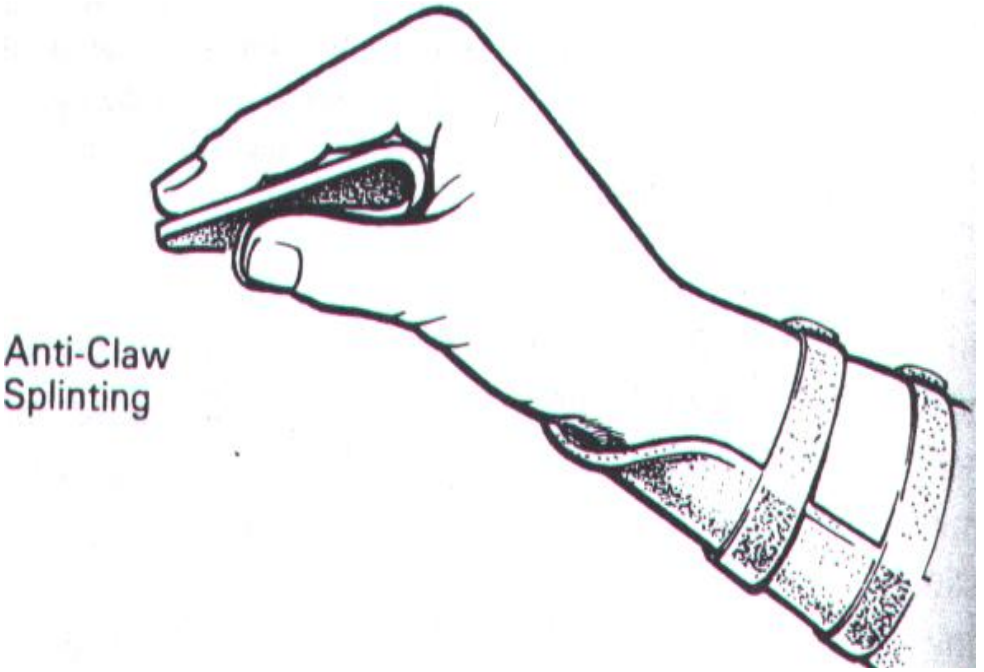


Illustration No: 5. The functional position of splinting [13].

Local wound care:

Large superficial burns require hospitalisation. In young children and some adults, a simple bulky antibacterial agent covered with absorbent gauze is used so that the hand is supported and bandaged in a bulky dressing in the safe Edinburgh position. A splint should be used to hold the wrist in moderate extension and the limb elevated.

The dressings may be left undisturbed for the healing period and can be patched with additional absorbent gauze in areas where a little exudate soaks through.

More extensive soiling requires repeat dressings. When the hand has healed at 10 to 14 days physiotherapy rapidly restores movement.

In co-operative patients these exercises can be started at the onset and continued throughout the healing phase while the wound is observed by placing the hand in a plastic bag bandaged around the wrist.

Localised well-demarcated full-thickness burns should be excised under tourniquet onto viable tissue and grafted. The hand is splinted in the functional position until the graft has taken and then is remobilised.

Deep partial thickness or deep dermal burns commonly affect the dorsum of the hand and their management is controversial [15].

Supporters of early excision around 4 days show that this approach speeds healing and reduces the length of stay in hospital. It may also produce a better scar and allows early mobilisation.

The conservative approach is safer for those who are not experienced in the diagnosis of deep dermal burns or in the technique of tangential excision (TE).

The burned hand is enclosed in a plastic bag with a suitable antibacterial agent and physiotherapy started immediately. The burn often takes more than 3 weeks to heal and some degree of scar hypertrophy is inevitable.

The use of pressure, particularly by elastic gloves is beneficial for hypertrophic scars and need to worn for 6 to 12 months (Illustration No: 6).

Extensive full-thickness burns are harder to treat and the outcome is less satisfactory. They are frequently associated with large body burns which limit the available donor sites for skin grafts. Some initial caution is worthwhile and delay may make a decision about treatment easier.

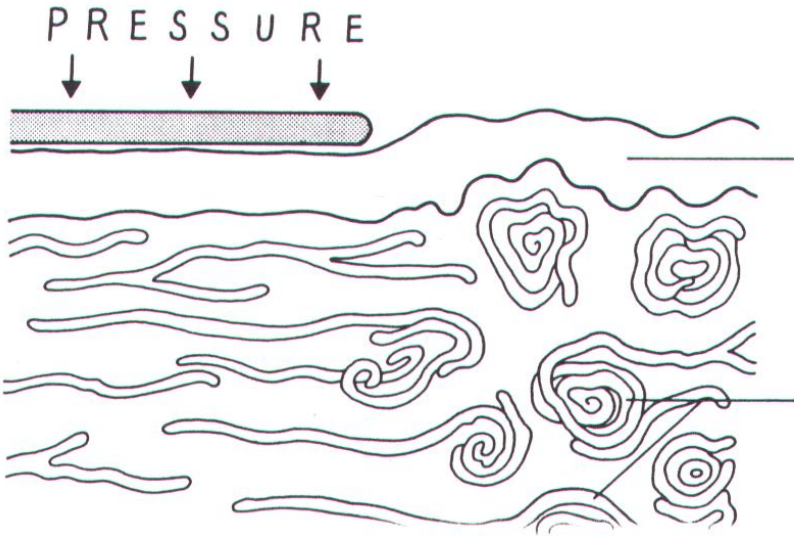


Illustration No: 6. The role of pressure in the treatment of deforming scars and contractures.

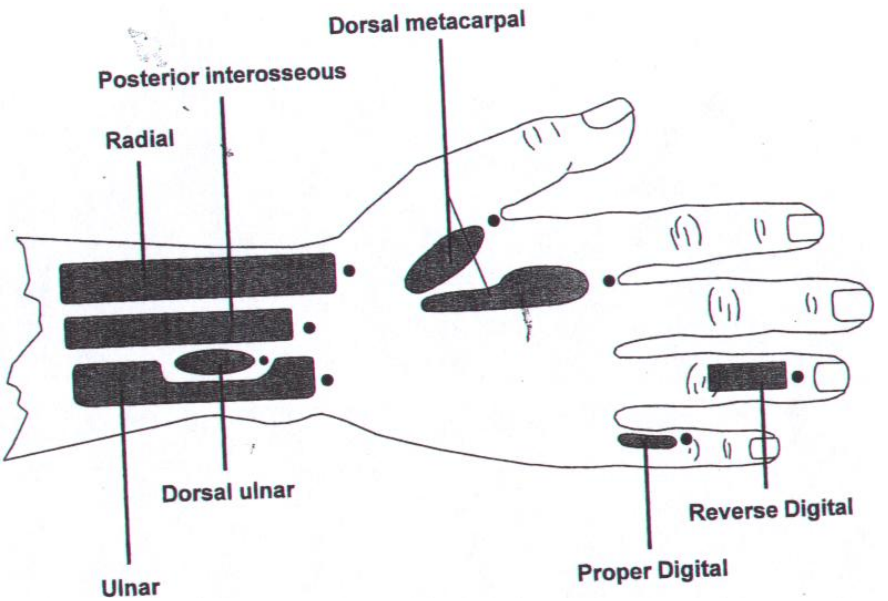


Illustration No: 7. Schematic of currently defined proximal donor skin territories, also useful as distal - based flaps for coverage of hand and fingers. Point of rotation would then coincide with distal vascular pedicle denoted by solid circles [32].

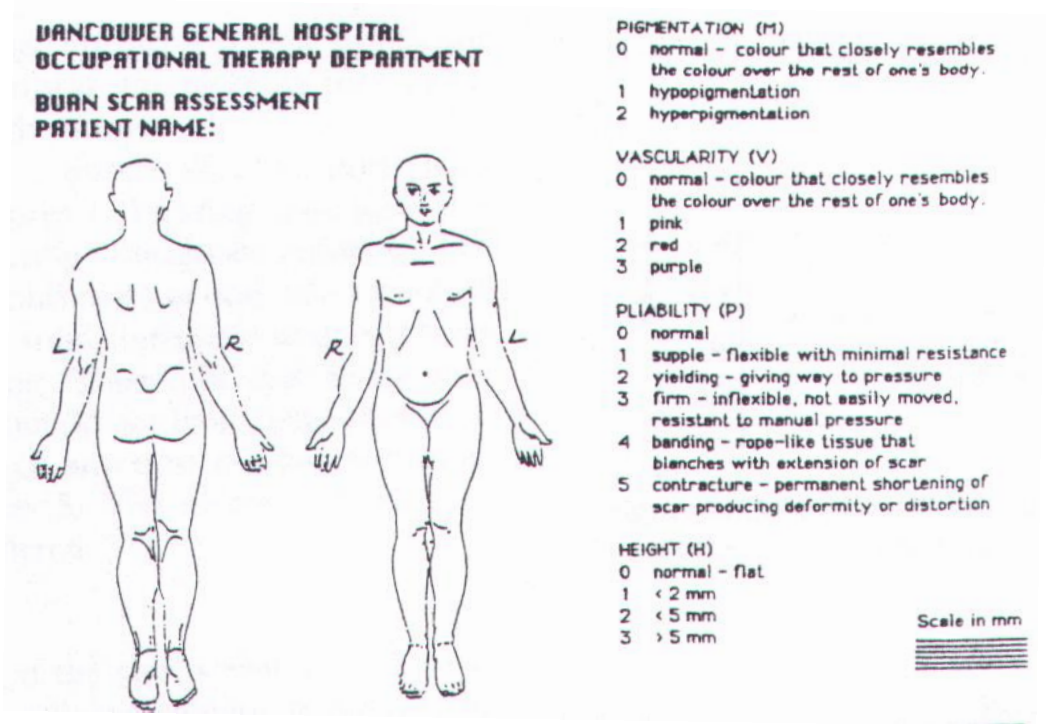


Illustration No: 8. The burn scar assessment form [43].

When burns are very deep and excision exposes avascular structures, flap coverage is necessary (Illustration No : 7). Small defects may be covered by local flaps but these are often unavailable or unreliable burned hands and, when large areas are involved, distant flap cover will be needed (Illustration No: 8).

Free flaps are also useful for localised areas of deep burns where adjacent undamaged vessels are available for microvascular anastomosis.

Where extensive skin grafting is required and donor sites are limited, early coverage of hand burns carries a high priority. In these circumstances the surgeon may use homografts or cultured skin with or without a variety of biological dressings.

These include acellular dermal matrix (Alloderm), bilaminate skin substitutes (Integra), and bioprosthetic dermal analogues (Biobrane). Although all of these dressings will promote wound healing, they will require definite replacement with epithelium.

Mesh grafting is another valuable technique but is less acceptable in the hand as the inevitable secondary epithelialisation between the mesh is unsightly and produces hypertrophic scarring (Illustration No: 9).

TYPES OF DEFORMITIES

A classification schema for upper extremities burn deformities and probable indicated procedures is described in Table No: 3 [12].

Claw Deformity

The position of comfort for the burned hand is metacarpophalangeal extension, proximal interphalangeal joint flexion, wrist flexion and thumb adduction.

These are also the positions of deformity and will lead to a "claw hand".

Most burns involve the dorsum of the hand and the thin skin overlying the extensor mechanism. This puts in particular danger the proximal interphalangeal joints.

This problem combined with the greater strength of the flexor mechanism, may lead to extensor tendon rupture. Likewise, the interphalangeal joint may be exposed.

The interphalangeal joints should be maintained in extension for several reasons.

These joints have no secondary support if surgical release becomes necessary.

Second, the collateral ligaments of these joints are tight in both extension and flexion.

However, the volar plate readily becomes fixed if the joint is allowed to remain in flexion and the pressure of the tight eschar over the central slip of the extensor tendon can cause erosion and rupture of the tendon, resulting in a boutonniere deformity that is almost impossible to reconstruct.

The metacarpophalangeal joints are eccentric in their axis of rotation. Therefore, the collateral ligaments are relaxed in extension and stretched in flexion.

If the joints are not flexed, the ligaments permanently contract producing an extension deformity [26].

Table 3.

TYPE OF UPPER EXTREMITY DEFORMITIES	PROBABLE INDICATED PROCEDURE
A. CLAW DEFORMITY 1. Complete 2. Incomplete	-Release and SG -Arthrodesis PIPJ
B. PALMAR CONTRACTURES	- FTSG
C. WEB SPACE SYNDACTYLY 1. Web space contracture 2. Adduction contracture 3. Syndactylism	- Release and local flaps - Release adductor pollicis and 1st dorsal interosseous
D. Hypertrophic and contracture bands	- Release and SG
E. AMPUTATION DEFORMITY	- First web release - Rotational osteotomies - Digital transposition - Toe – to – hand transfer
F. NAIL BED DEFORMITY	
G. ELBOW AND WRIST 1. Flexion contracture 2. Deep extensive tissue loss 3. Heterotopic ossification	- Release and local muscle, fasciocutaneous or free flap
H. AXILLA	

A boutonniere deformity can result when the central slip of the extensor mechanism has been destroyed initially or during the healing phase.

When this occurs, the lateral bands shift volarly to become proximal interphalangeal joint flexors rather than extensors (Plate 7). Next, the absence of the central slip creates a loss of restraint for the extensor mechanism that allows this system to move proximally. This results in excessive pull on the distal interphalangeal joint through the lateral bands and subsequent hyperextension of the distal joint.

Extensive tissue injury and poor skin coverage usually eliminate the possibility of an anatomic repair of the central slip. No fully satisfactory treatment exists, although multiple solutions have been proposed [27], [28].

Web Space Contractures

Web space contracture is the most common web space deformity after burns. It is a scar involving the dorsal aspect of the web space. Excellent therapy, early surgery and cooperation from the patient not withstanding, this type of contracture is still frequently seen.

Effective pressure in this area is difficult to obtain, but surgical treatment is not difficult. The V-Y plasty is preferable. The primary advantage is that the flaps are not separated from the underlying tissue. They are not shifted in regard to their circulation and because of this, scar tissue can be used in the reconstruction (Illustration No: 9).

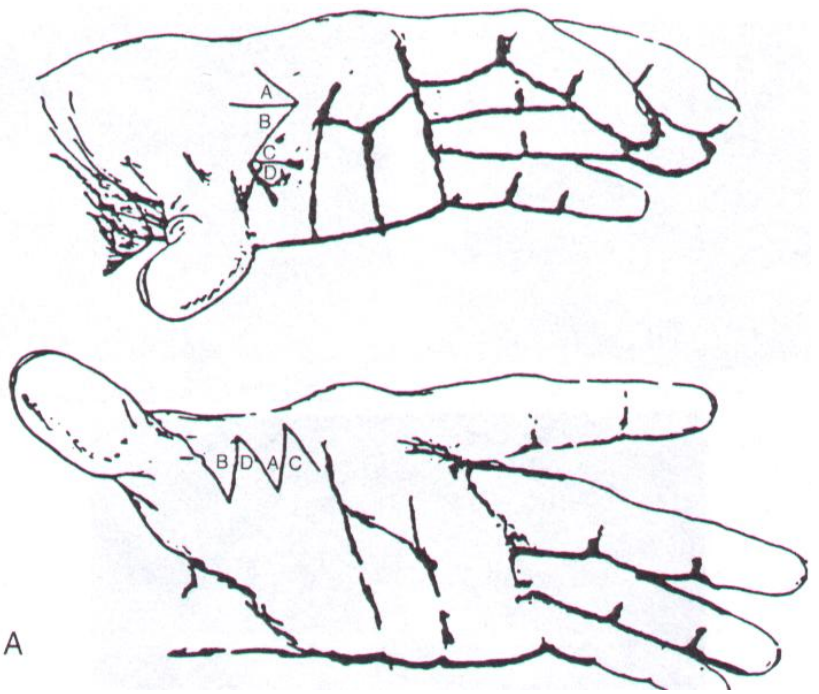


Illustration No: 9. The four limb Z – plasty, a commonly used method for correction of first web space contractures [6].

Adduction Contracture

An adduction contracture involves the first web space and usually entails fibrosis of the adductor muscle and first dorsal interosseous. A web space contracture involves skin only, whereas an adduction contracture include muscle fibrosis.

For release of this contracture, some fascia and muscle must be divided.

Burn Syndactyly

Burn syndactyly is very rare. In severe cases the fingers are actually fused (as seen in congenital syndactyly) with no intervening skin.

Skin grafts as well as local flaps are required to correct this deformity [29].

Hypertrophic Scar and Contractures

Scar bands may occur at any injured part of the hand. After a burn injury, all the scars become thick, red, tight, pruritic and relatively unyielding.

This process worsens during the first 3 to 6 months post injury. Somewhere in this period the forces plateau and then begin to improve.

Eventually the scars become purple and then more supple with a more normal skin colour. The itching abates and a mature scar results. This entire process usually takes a year, and in a burn patient it can take longer [30], [31].

Hypertrophic scarring may interfere with function depends on lifestyle, work or hobbies. Release and resurfacing should be done as needed. Ideally one would like to wait for the scars to mature before embarking on any reconstructive procedures, but this is not always practical.

Any time a scar contracture of the hand is subsequently released or the hand is resurfaced, a splint must be placed and worn until the graft is stable.

It may be removed during the day for activities but should be replaced at night.

Compressive garments and gloves (for example Jobst) may also be indicated to prevent hypertrophic scarring. All deep or grafted burns should be placed in elastic compressive garments for 12 months.

Flaps are employed when skin grafts are unsuitable. Early free flap reconstruction may be necessary after extensive debridement but this approach can present problems in that local vessels may be damaged. This may necessitate vein grafting to more distant vessels to ensure viability of the free flap transfer.

For deep burns in which there is no viable perdition or eriostemon, flap coverage is necessary. Local flaps are used when possible.

Indications for flaps instead of grafts include: [26]

1. The recipient site is unsuitable (not enough vascularisation) for graft survival.
2. Subsequent reconstruction is planned for which subcutaneous tissue replacement as well as good skin is required (for example future tendon grafts).
3. When vital structures must be protected with adequate soft tissue.

The temporoparietal fascial free flap is particularly useful in the hand for smaller defects. Other options are a lateral arm free flap, if available, and muscle free flap such as the serratus or latissimus dorsi. The standard pedicled groin flap is often useful for extensive injuries in the hand [32], [33], [34], [35], [36].

If a joint has been immobilised by a scar band, a release may have to be performed before the scar is mature. Also, when one determines that a scar is never going to be acceptable and the entire scar would be removed during the reconstructive procedure, this can be done well before maturation occurs.

Hands are treated with excision and repair with local flaps if possible.

If a large area has to be excised, a graft may be required. For small areas, a full thickness graft is performed. Mesh grafts are not typically used in reconstructive surgery.

Amputation Deformities

Amputation deformity is a result of the most severe injuries.

Patients who have extensive burns or electrical injuries are the most likely to have an amputation deformity.

Numerous reconstructive procedures are available to restore function following digital amputation. Phalangization is a procedure that can effectively lengthen fingers and thumbs by deepening the web spaces.

Not only the digits appear longer, they also have wider range of motion and function. This procedure is an exaggerated web space correction.

Thumb Reconstruction

The adequacy of soft tissue coverage must be assessed first. If soft tissue coverage is not adequate, flap coverage of the area of the first metacarpal and web space should be undertaken as a first stage. This can be done with a groin flap or a free flap, depending on the availability of unburned tissue in various sites.

Pollicization should be considered when the thumb doesn’t have sufficient length to oppose the remaining digits [9], [37], [38], [39].

A severely damaged thumb and a ray (which will have the MPjoint and a small remnant of the proximal phalanx) can be combined to make a very useful thumb, as well as eliminate the damaged digit that was in the way.

Before the pollicization procedure, the skin coverage of the hand should be evaluated.

If better coverage is needed, the hand should be resurfaced with a groin flap or a free flap. Free scapular fascial flaps, intercostals cutaneous perforator flaps, local fasciocutaneous flaps and / or fasciocutaneous cross-arm flaps have all been described for this purpose.

Distraction osteogenesis [40] of burned metacarpal was first described by Mater and later by Stern for the thumb metacarpal. This technique should be considered when increased length would be helpful. The family needs to understand the programme and how to do the distraction at home.

Nail Bed Deformity

Eponychial retraction and proximal nail exposure are caused by dorsal digital burn contractures. These areas are subject to repeated break down resulting from normal activities or trauma to the hand. Numerous flaps have been described.

A one-stage reconstruction with bilateral proximal flaps dorsally transposed and interdigitade is recommended [13]. This requires two flaps. They should be narrow so that the donor site can be closed with sutures. The flaps are curved to fit the curve of the nail fold.

Wrist and Elbow

Elbow contractures are common in patients with very extensive life threatening burns. Range of motion needs to be maintained in the elbow, as with all joints.

The elbow is, unusual however, in its tendency to form heterotypic ossification.

It typically occurs in patients with very severe burns. They may result from overzealous therapy. Heterotopic ossification is difficult to treat once established.

Early proper splinting is important in prevention of elbow contractures.

The elbow should be splinted virtually straight during sleeping. If elbow contractures can not be prevented by splinting, they can be repaired by release of the contracture with coverage by STSG.

Axilla

Early coverage of the axilla helps prevent contractures. Pulleys or other devices should be made available for patients in the acute phase and in therapy to maintain active range of motion across this joint.

Differences between the elbow and axilla are that the elbow is relatively easy to splint and recurrent contractures of the elbow are uncommon.

The axilla is very hard to immobilize and more difficult for graft take because of its irregular contours. Consequently, if a skin graft is used, recurrence of contracture is common and immobilization and therapy are cumbersome and prolonged.

Fortunately, a regional flap such as the latissimus dorsi fasciocutaneous flap is very useful.

If the axilla is burned extensively from anterior to posterior axillary line, the release produces a large defect. The only choices are sheets of STSG or flaps.

Flaps are unsuitable because they are too thick and redundant.

If the only problem is a linear contracture band along the anterior or posterior axillary line and there is unburned skin on one or both sides of the band, a local flap, simple Z- plasty or even a triangular transposition flap can eliminate these with quite satisfactory outcome.

Care must be taken to do a complete release. Local flap are also preferred versus SG.

B. AIM

In this study we aim to evaluate the outcomes of patients with burn' s hand injury that were treated at the University Hospital of Birmingham Burns and Plastics Unit. The following parameters were included:

Table 4. A planned treatment program

EVALUATION :	
- *Superficial 1st degree*	Treatment – rehabilitation
- *Superficial 2nd degree*	Elevation – splint – exercise – rehabilitation Heal by re-epitheliazation / Hypertrophic scars managed by PG / operations
- *Deep 2nd degree and full thickness burn*	Excision – grafting – early rehabilitation

I. Clinical Outcomes

In the present study, after providing to all the patients a planned treatment programme, (Table No: 4) the clinical outcomes that were recorded and evaluated were:

- Male / Female ratio
- Cause of burn
- Most common type of burn
- Associated injuries
- Previous pathology/predisposing factors
- Severity of burn
- Percentage of body surface area burned
- The burn depth and whether this was not reported (missing admission charts because of referrals / no records of depth)
- The age at the burn injury / most common age group
- Deformities following acute treatment
- Number of early shaving and skin grafting
- Management of chronic deformities
- Number of contractures released
- Patient's age at first release
- Total number of releases according to method of release
- FTSG / STSG
- Donor sites FTSG / STSG
- Donor site morbidity
- Graft site morbidity
- Complications

- Effect of growth on contracture releases (Age groups: 0-2, 2-6, 6-10, 10-14, 14-18, 18-21, >21)

The age of 21 years old is the time that linear growth should have ceased [38].

Contractures are produced not only by skin loss but also by the differential growth rate between the burn scar and the rest of the adjacent normal skin and tissues.

Growth occurs in 3 phases:

There is a rapid phase of growth in infancy and in some premature babies extending to the second year. This is followed by a marked deceleration of growth.

Then there is a steady but slower rate of growth between 2 and 10 years of age, with a gradual further decline in rate in the propubertal years.

Finally, in the third (or pubertal phase), growth is rapid. Late maturers will continue physical growth up to the age of 19 to 21 years of age.

II. Functional Outcomes

The therapist recorded range of motion of the hand at each clinical visit.

For the study, the range of motion at the most recent clinic visit was recorded [8].

Range of motion was graded as;

0. Full: Normal ROM with full extension of all digits and thumb abduction to 50 degrees or better

1. Good: Hands with contractures of 5 degrees on any flexor surface or evidence of banding or webbing
2. Fair: Hands with flexion contractures from 5 to 30 degrees
3. Poor: Hands with flexion contractures over 30 degrees

- *Ability to perform or not activities was reported:*

a) at work
b) at leisure
c) activities of daily living
   - sleep
   - carrying
   - lifting
   - shopping
   - driving
   - cleaning
   - Pain
   - Sleeping disturbances
   - Mental situation

Finally the injury category and the outcome category were evaluated as illustrated in the following schema (Table No: 5).

Table 5. Injury and outcome categories

Injury and Outcome Categories :		
Injury Category		
	I	Second – degree burn that healed without surgery
	II	Deep – degree burn that required surgery but did not involve underlying bone
	III	Deep – degree burn involving bone and requiring fixation
Outcome Category		
	A	Normal function
	B	Abnormal function but able to perform activities of daily living
	C	Hand can not perform activities of daily living (feeding – toileting)

C. PATIENTS AND METHODS

A retrospective review was carried out of the case notes of all 22 patients who received treatment for hand burns at the Burns Unit, Selly Oak Hospital, Birmingham and were reviewed in the outpatient clinics between October 2000 and February 2001, to evaluate our experience.

The case notes included the clinicians' and nurses' entries during the patients' admission, outpatient clinics (dressings clinic and main) and correspondance with the general practitioners (family physicians).

The dressings clinic is a daily clinic (within the Burns Unit) for reviewing patients with recent burns and burns-related operations who were being managed as outpatients or had been recently discharged from the ward.

Information was obtained about the burn injury, contracture site, interval between burn and release of contractures, indication, age at first release, intervals between releases, operative details (donor and graft sites), complications and non operative treatment, and follow up to the end of the study.

Certain points of particular relevance to post burn contracture release were taken into consideration. These included anaesthetic considerations, need for meticulous dissection because of the distorted anatomy, scrupulous haemostasis, adequate immobilisation.

The patients in the study were seen at regular intervals, some were seen more frequently, because of particular problems / concerns.

Physiotherapists and occupational therapists were involved at all stages, splints applied after releases, e.g. around joints to maintain maximum release while the graft takes and left in place until mobilisation commences.

Depending on the mobility of the joint or clinical evidence, of a tendency of the contracture to recur, the splints were left in place for a variable period, varying from a few weeks to 6 months for some occasions.

Other non operative treatment used included massage, pressure garments and cosmetic camouflage.

Pressure garments were used when deemed necessary (such as in hypertrophic scarring after a recent burn or surgery).

Superficial burns that were managed as outpatients and patients who refused treatment were excluded from the study.

Table 6. Age distribution of patients with hand burns

Age of patients with burned hands Age (yrs)	Patients No	%
1	*3*	13,6
1-10	*10*	45,4
11-20	*3*	13,6
21-40	*3*	13,6
41-60	*3*	13,6
	22	

Table 7. The injury mechanism, gender distribution, age, TBSA and number of operations

Mechanism of injury	*No*	*(M/F)*	*AGE (yr)*	*TBSA burn%*	***Operations***
Electrical	*2*	*M*	*35*	*10%*	*9*
		M	*13*	*24%*	*2*
Contact burn	*4*	*F*	*1*	*1%*	*1*
		M	*2*	*1%*	*4*
		M	*57*	*1%*	*1*
		M	*1*	*1%*	*3*
Flame burn	*6*	*M*	*3*	-	*2*
		M	*6*	*20%*	*5*
		F	*6*	*10%*	*0*
		F	*18*	*13%*	*4*
		M	*14*	*23%*	*10*
		M	*28*	*42%*	*0*
Chip pan fire	*1*	*M*	*54*	*4%*	*2*
Scalds	*7*	*M*	*5*	*38%*	*1*
		M	*1*	*1%*	*1*
		M	*0,8*	*10%*	*4*
		M	*2*	*6,5%*	*0*
		M	*2*	*2%*	*1*
		F	*2*	-	*7*
		M	*3*	*10%*	*4*
Flash burn	*2*	*M*	*21*	*1%*	*1*
		M	*54*	*8%*	*1*
	22				

D. RESULTS

A total number of 22 patients were included in the study – 18 males and 4 females; 16 patients were children and 6 were adults (Table No: 6).

The mean follow up period was 5,8 years. Most common age group in children was 4,5 years old and in adults was 38,1.

The mean percentage of body surface burned was 10,8 %. In 4 patients the depth of the burn was reported as FT and in 6 as PT.

In 5 patients there was no report of depth and in 7 patients the admission report was lost, because of delayed admission.

Most common type of burn in children was scalds (Table No: 7).

The interval between burn injury and first release was 5,3 years. The total average number of releases per site : 1,7.

Number of releases after SSG: 6 and after FTSG: 1.

Z-plasty was used in 8 cases, FTSG in 7, STSG in 12, W-plasty in 8 (Tables No: 8, 9, 10, 11).

Table 8. Results of motion evaluation

Results of motion evaluation EVALUATION Full ROM ROM Score (median)	 *FULL-THICKNESS* *7* *1-2*	 *SPLIT-THICKNESS* *12* *1*
Surgical releases	*1*	*6*

Table 9. Effect of growth on contracture releases

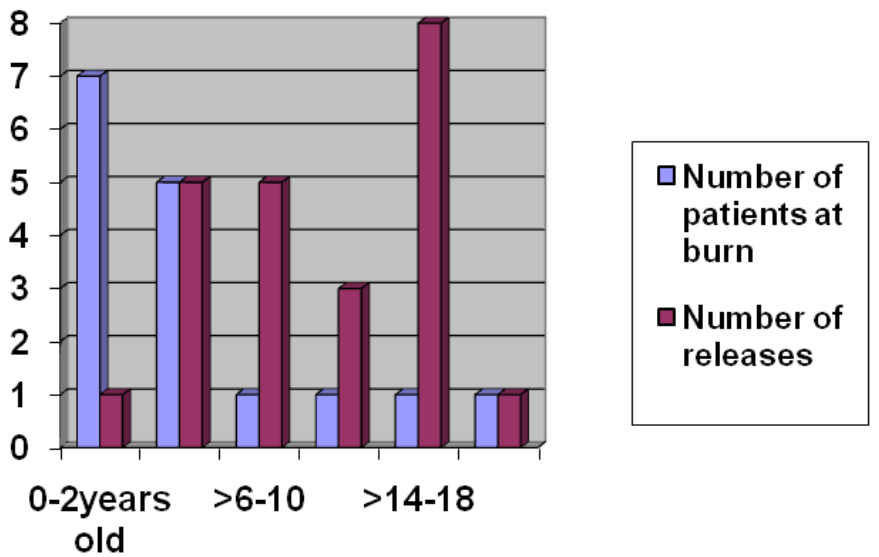


Table 10. Number of releases according to method of release

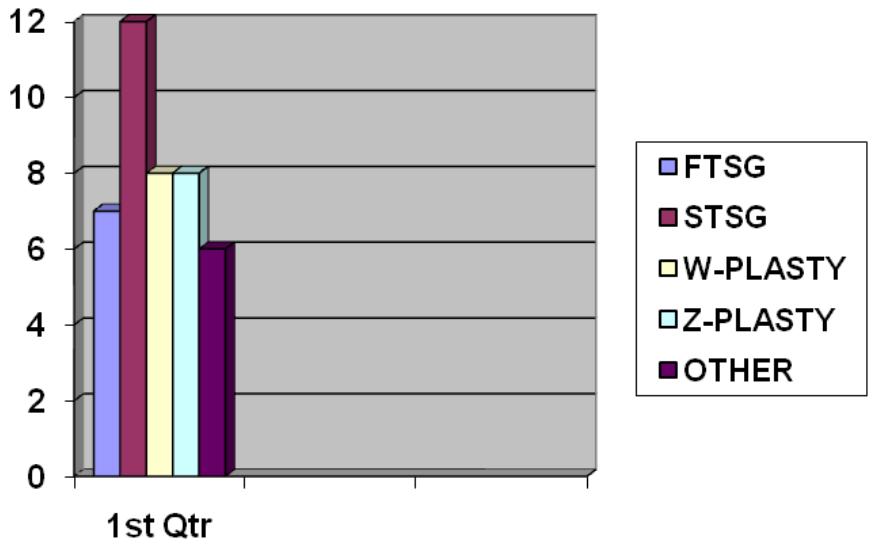
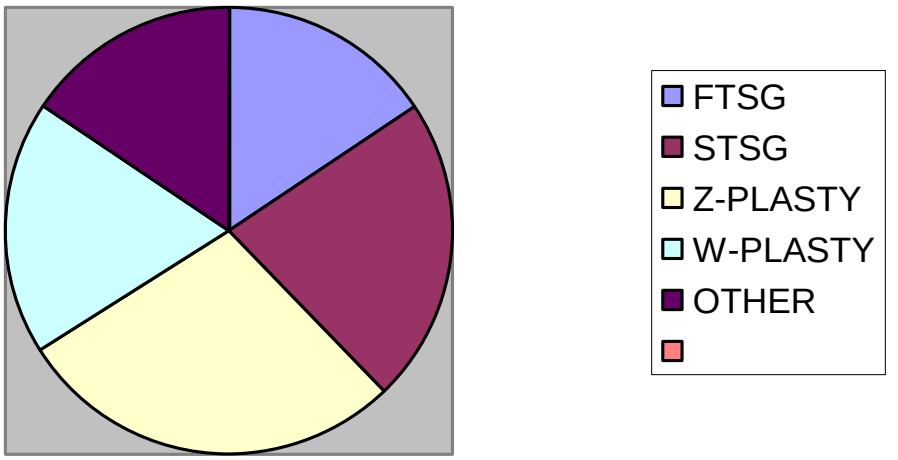


Table 11. Total number of releases according to method of release (distribution of releases by different techniques during the period of study)



History / tendency to keloids formation was reported in 2 patients.

3 patients had post – traumatic stress disorders / sleep disturbances / flashbacks (Table No : 12).

The only predisposing factor that was referred was epilepsy in 2 adults.

The ROM was full in 10 hands, good in 10 hands and fair in 3. According to the correlation of the injury and outcome category : IA: 2, IIA: 8, IB: 1, IIB: 9, IIC: 3 (Tables No: 13, 14).

Most common donor site form FTSG was the groin area and for STSG the thigh.

3 patients developed infection of the donor area but with satisfactory final aesthetic result.

5 patients developed infection of the grafted area that had as a result partial failure of the graft in 2 cases.

10 patients complained of hypertrophic scarring of the grafted site that responded in treatment with PG and silicon gel sheets, while 5 patients complained of rash, itching and pruritis of the graft.

Table 12. List of complications

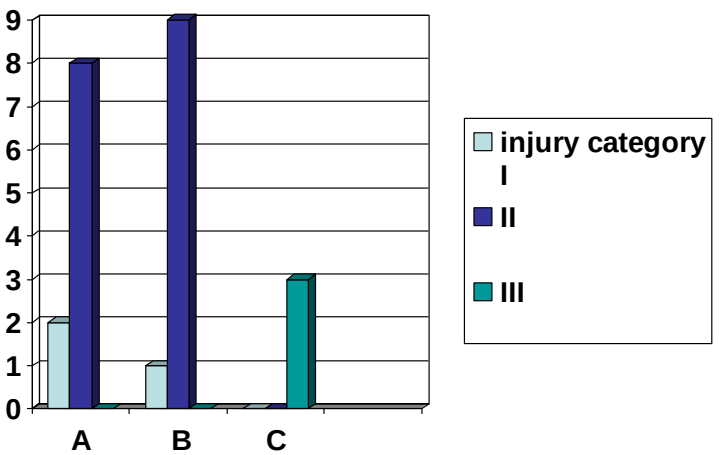
COMPLICATIONS	
Donor site infection	*3*
Graft site – infection	*3*
-over granulation/hypertrophic scarring	*10*
-rash / pruritis	*5*
Sepsis / ARDS	*1*
Pneumonia	*1*
Amputation	*2*
Post-traumatic stress disorders	*3*
Nail bed deformity	*1*
Elbow heterotopic ossification	*2*
Keloids	*2*

Table 13. Functional outcome in patients stratified by injury category

Injury category	*Total number of hands*	*Required reconstruction*	*Functional category A B C*
I	3	4,3 %	2 1 0
II	17	60,8 %	8 9 0
III	3	4,3 %	0 3

I: Non surgical therapy group.
II: Non fourth degree / surgically treated.
III: Fourth degree / surgically treated.

Table 14. Functional outcome in patients stratified by injury category



D. DISCUSSION

As the upper extremity is frequently burned either in isolation or in combination with other parts of the body, it is cumbent on the burn surgeon to organise a multi-disciplinary team, patient controlled approach, with the concepts and execution of appropriate treatment protocols. With such a team, consistent results achieving maximum potential can be obtained for a patient with a burned upper limb.

The findings from the study suggest that although a well-designed prospective study is needed to assess the magnitude of contracture, aesthetics, function and complications after hand burns, the results are in agreement with the literature reports [41], [42].

The use of skin grafts for post burn contracture release is simple, reliable and safe. They are particular useful for an extensive area of release. Their main disadvantage is tendency to recontracture, necessitating further release, which is less a problem with FTSG.Whenever possible, the use of FTSG is recommended in preference to STSG in post burn contracture release.

For the same site, release with STSG was associated with more releases of the contracture than with FTSG.

The interval between the initial release and first release was shorter than with FTSG.

Patients reported more satisfaction with texture and colour match with FTSG.

There was comparable donor site and graft morbidity with both types of grafts.

All patients were able to perform activities of daily living and were generally satisfied.

The children required more procedures during growth spurts, reflecting the differential effect of the growth of normal skin and contracture tissue.

It is clear that reconstruction of paediatric hand burn is a complicated task and attention to details during the acute phase of injury may be surgeons' greatest ally in subsequent functional rehabilitation of the hand.

Reducing oedema, maintaining digital circulation, limiting inflammation, and mobilising the limb early are key parameters to assure return of function during the acute phase of injury [43].

Although children may present with neglected contractures at a later date, contractures can be surgically approached with hopes of improving hand function.

A more aggressive surgical approach, with increased optimism, therefore is required when addressing children with complex hand burns requiring reconstruction.

Accordingly, the need for reconstruction can be minimised, and functional outcome improved for these patients.

To summarise, a coordinated plan of care of acutely burned hands can lead to a high quality survival after burn injury. This can be achieved only with early burn management and after burn injury.

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Chapter 4

THE ROLE OF APOPTOSIS IN BURN INJURY

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ABSTRACT

Apoptosis is a significant mode of cell death following reperfusion injury in burn wounds. The zone of stasis in partial thickness burn wounds is exposed to oxidative stress resulting from ischemia-reperfusion injury. Nitric oxide (NO) plays a significant role in the initiation of the inflammatory cascade following ischemia and oxidative stress during the reperfusion period. Recent results suggest that i-NOS inhibition in partial thickness burn wounds reduces apoptotic tissue injury in the zone of stasis. This therapeutic intervention may have clinical application for tissue preservation in the thermally injured patients. In this chapter we also give a comprehensive overview about the current knowledge and the key role of apoptosis in research innovations in the field of burn injury. Burn injury is a complex traumatic event with various local and systemic effects, apoptosis is affecting several organ systems beyond the skin. Recent advances in the comprehension of mechanisms underlying systemic complications of thermal injuries have contributed to uncover part of the cellular and molecular basis that underlie such changes. Recently, apoptosis has been considered playing an important role in the development of such pathological events.

Keywords: Burn injury, zone of stasis, apoptosis, wound healing

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INTRODUCTION

Apoptosis is defined as the process of programmed cell death that may occur in multicellular organisms. Biochemical events lead to characteristic morphologic cell changes and death. These changes include blebbing, cell shrinkage, nuclear fragmentation, chromatin condensation, and chromosomal DNA fragmentation (Figure 1). Unlike necrosis, apoptosis produces cell fragments called apoptotic bodies that phagocytic cells are able to engulf and quickly remove before the contents of the cell can spill out onto surrounding cells and cause damage.

In contrast to necrosis, which is a form of traumatic cell death that results from acute cellular injury, apoptosis, in general, confers advantages during an organism's life cycle. For example, the differentiation of fingers and toes in a developing human embryo occurs because cells between the fingers apoptose; the result is that the digits are separate. Between 50 and 70 billion cells die each day due to apoptosis in the average human adult. For an average child between the ages of 8 and 14, approximately 20 billion to 30 billion cells die a day.

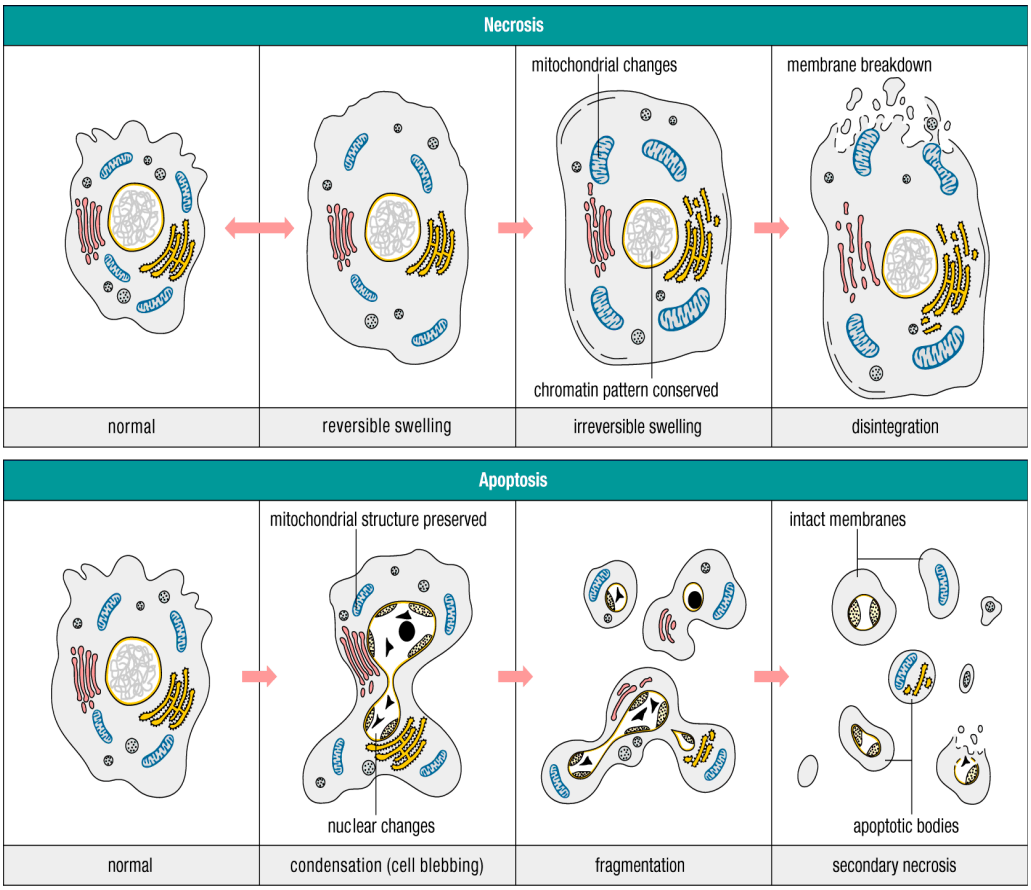


Figure 1. Comparison between cell death mechanism necrosis vs. apoptosis.

Research in and around apoptosis has increased substantially since the early 1990s. In addition to its importance as a biological phenomenon, defective apoptotic processes have been implicated in an extensive variety of diseases. Excessive apoptosis causes atrophy, whereas an insufficient amount results in uncontrolled cell proliferation, such as cancer.

The process of apoptosis is controlled by a diverse range of cell signals, which may originate either extracellularly or intracellularly. Extracellular signals may include toxins, hormones, growth factors, nitric oxide or cytokines, that must either cross the plasma membrane or transduce to effect a response [1,2]. These signals may positively (i.e., trigger) or negatively (i.e., repress, inhibit, or dampen) affect apoptosis.

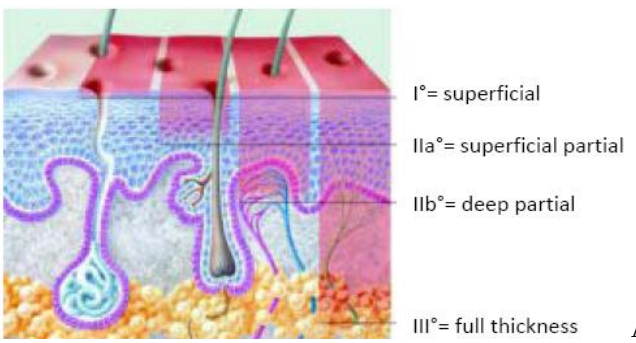
A cell initiates intracellular apoptotic signaling in response to a stress, which may bring about cell suicide. The binding of nuclear receptors by glucocorticoids, heat, radiation, nutrient deprivation, viral infection, hypoxia and increased intracellular calcium concentration, for example, by damage to the membrane, can all trigger the release of intracellular apoptotic signals by a damaged cell [3,4]. A number of cellular components, such as poly ADP ribose polymerase, may also help regulate apoptosis [5].

Before the actual process of cell death is precipitated by enzymes, apoptotic signals must cause regulatory proteins to initiate the apoptosis pathway. This step allows apoptotic signals to cause cell death, or the process to be stopped, should the cell no longer need to die. Several proteins are involved, but two main methods of regulation have been identified: targeting mitochondria functionality, or directly transducing the signal via adaptor proteins to the apoptotic mechanisms. Another extrinsic pathway for initiation identified in several toxin studies is an increase in calcium concentration within a cell caused by drug activity, which also can cause apoptosis via a calcium binding protease calpain.

Since 1995, numerous reports have begun to investigate the occurrence of apoptosis following thermal injuries. It immediately appeared evident that almost every organ or system was influenced directly by molecular mediators released from the burn site or indirectly from pathophysiologic and cellular changes secondary to burn consequences on the organism.

BURN WOUNDS

Burn wound depths are internationally classified in the degree I-III (Table 1). The following figures present a histological overview as well as clinical pictures of various burn wound depths (Figure 2).



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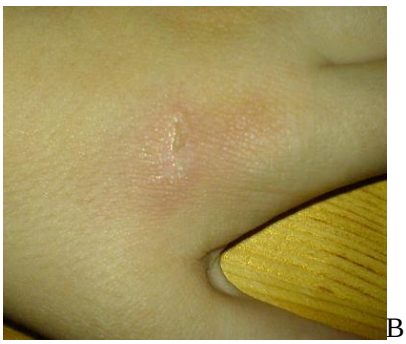
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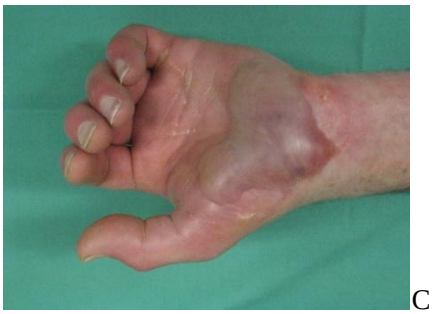
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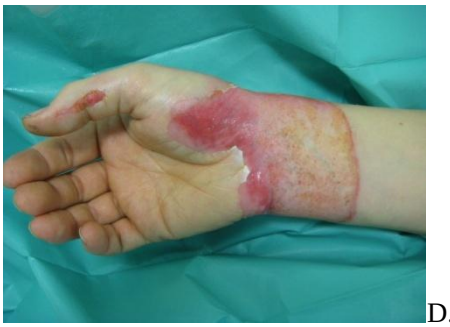
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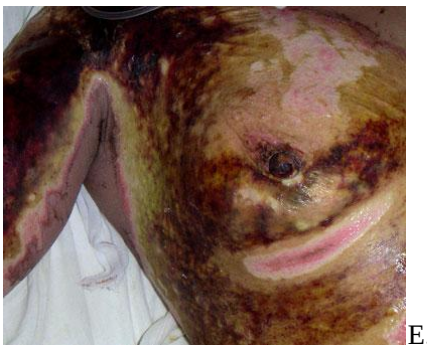
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Figure 2. classification of burn wound depth. A) histologic overview, B-E) clinical examples of burn degrees B) superficial=I°, C) superficial dermal=IIa°, D) deep partial=IIb, E) full thickness=III°.

Table 1. description of clinical characteristics of burn wounds of various depth

Degree/ Depth	Aetiology	Layer of skin involved	Appearance	Pain	Healing time
Superficial I°	Sun exposure, hot liquids with low viscosity and short exposure	Epidermis only	Pink to red, moist, no blisters	Moderate-Severe	3-7 days
Superficial partial IIa°	Hot liquids, chemical burns with weak acid or alkali, flash	Superficial (papillary) dermis	Blister, red, moist, intact epidermal appendages, blanches of pressure	Severe	1-3 weeks, long-term pigment changes may occur
Deep partial IIb°	Flame, chemical, electrical, hot liquids with high viscosity	Deeper layer (reticular) dermis	Dry, white, non-blanching, loss of all epidermal appendages	Minimal	3-6 weeks, with scars
Deep III°	Flame, electrical, chemical, blast, self immolation	Full thickness of skin and in to the subcutaneous fat or deeper	Leathery, dry, white or red with thrombosed vessels	No	Does not heal by primary intention, requires skin graft

The depth of burn wound evolves over time especially with partial thickness wounds. Wounds that start as superficial partial or deep partial burns may progress to deep partial or deep burns over period of 2-4 days after burn injury. As evidenced by histologic studies, burn injury is a dynamic process that peaks at about 3 days. Necrosis in the zone of stasis has been thought to be responsible for this progression. Recently, apoptosis has been recognized to be present in the zone of stasis and may contribute to the wound progression [6]. Due to this unique pathophysiology, patients with partial thickness burn wounds need to be evaluated for depth of the wound periodically. As a rule, partial thickness burns that are predicted not to heal by 3 weeks should be excised and grafted. A potential new promising tool in evaluation of indeterminate burn wound depth could be an innovative multispectral optical system, which enables a parallel acquisition of spectrally filtered images and allows to depict burn degrees [7].

Local Effects of Burn Injury

Through molecular structural alterations toxic metabolites as well as antigens and immunomodulatory agents are released resulting in burn shock pathophysiologic effects. The local mediators released are histamine, serotonin, bradykinin, nitric oxide, oxygen free radicals and products of eicosanoid acid cascade (prostaglandin, thromboxane), TNF, interleukins. Histamine is most likely to be the mediator most responsible for the early phase of increased microvascular permeability seen immediately after burn. Histamine causes large endothelial gaps to transiently form as a result of the contraction of venular endothelial cells.

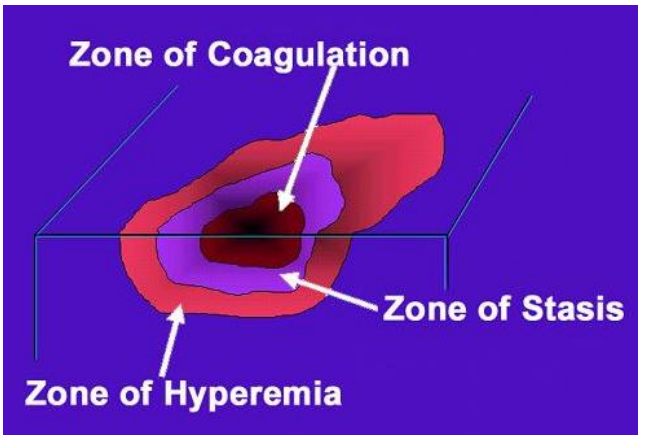

Figure 3. zones of burn injury.

Studies demonstrated that the pathogenesis of burn edema in the skin appears to be related to the interaction of histamine with xanthin oxidase and oxygen radicals [8].

The local changes in burn wounds are classified by *Jackson* into 3 zones (Figure 3) [9]:

The zone of coagulation at the central focus of injury is generally thought to consist of devitalized tissue. The most peripheral zone is termed the zone of hyperemia, characterized by vasodilation, inflammatory changes without structural damage. Between these zones, an intermediate region of indeterminate prognosis arises which is termed the zone of stasis [9]. The zone of stasis is often best identified in mid to deep dermal burns and represents a region of vascular stasis and ischemia. From a clinical perspective, it is this region which poses some of the greatest challenges for the burn team. This tissue has the potential to heal or alternatively to progress to a full thickness lesion. Clinically this ischemic area can only be salvaged, if revascularization is achieved within a few days. Otherwise the irreversible tissue death is inevitable. The phenomenon of ischemia-reperfusion events in the zone of stasis has been described in the past [10]. This zone is exposed to oxidative stress resulting from reperfusion injury, particularly after sustaining major partial thickness burns. Reperfusion injury results in predominantly apoptotic cellular death. The apoptosis in the zone of stasis may contribute to progressive tissue loss. Previous studies showed a reduction of the apoptotic rate after inhibition of inducible NO-synthase in partial thickness burn wound [11].

Nitric Oxide and Burn Injury

Nitric oxide (NO) plays a significant role in the initiation of the inflammatory cascade, notably from increased expression of macrophage inducible nitric oxide synthase (i-NOS) and is pertinent to burn pathophysiology [12,13]. NO is produced by endothelial cells from amino acid L-Arginin, the release is mediated through NO-synthase (NOS) (Figure 4). The inducible form (i-NOS) is normally not synthesized; it's released by inflammatory cytokine and endotoxin [14]. Nitric Oxide is known to be very reactant. Even more tissue destroying substances are produced from the origin NO, like Peroxynitrite as well as reactive oxygen species (ROS) [14]. Evers et al. designed an experimental study to develop an animal model of apoptotic cell injury in a mouse deep partial thickness burn injury [11].

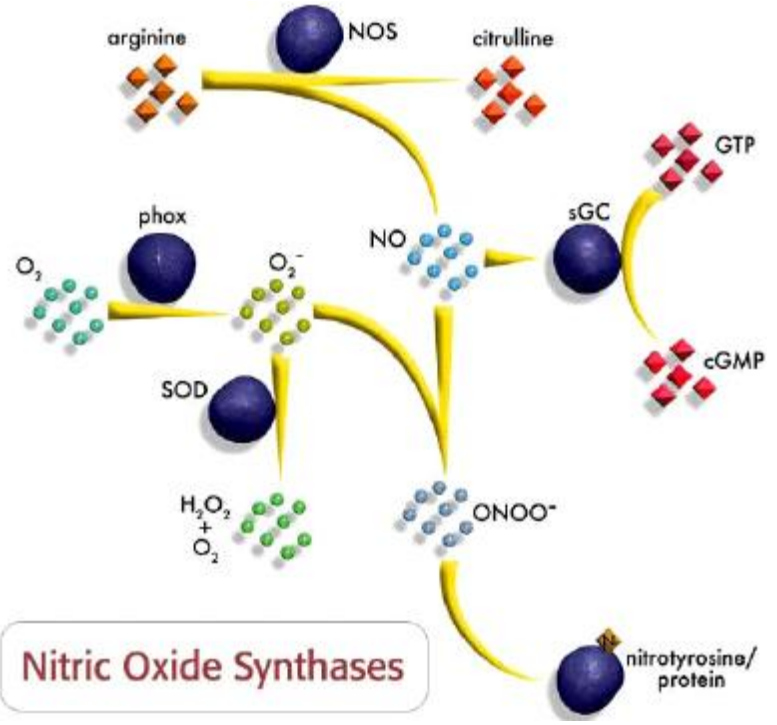

Figure 4. Overview of the role of Nitric Oxide.

The hypothesis of this study was by inhibiting the inducible NO-synthase they may reduce apoptotic cell death in the zone of stasis. They also investigated the possible protective effect of a specific i-NOS inhibitor against apoptosis in partial thickness burn wound. In this study 40 mice received a 30 % TBSA dorsal scald burn. All groups received standard intraperitoneal resuscitation and analgesia. Control group (n=20) received no additional interventional medicines. Study group (n=20) received 3 mg/kg i.p. S-methylisothiourea (SMT), a specific i-NOS inhibitor every 12 hours. 10 animals in each group were sacrificed at 24 h and 48 h. The visible burn wound and adjacent tissues were included for analysis to assure incorporation of all zones of injury. The histologic review was performed by a study blinded investigator/pathologist. The objective TUNEL assay, M30 Cytodeath assay and calculation of the apoptotic index were similarly performed. The mean apoptotic index (AI) for control group was 0.248 (± 0.04 SE) and 0.181 (± 0.02 SE) at 24 and 48 hrs respectively. The AI for the i-NOS inhibitor treated group was 0.147 (± 0.03 SE) and 0.141 (± 0.06 SE) at 24 and 48 hrs respectively. The difference between the groups was statistically significant (ANOVA, $p<0.05$). With the M30 Cytodeath-assay epidermis and epithelial appendages verified the presence of apoptosis. The results suggest that i-NOS inhibition in partial thickness burn wounds reduces apoptotic tissue injury in the zone of stasis [11].

Zone of Stasis - Key Area of Tissue Preservation

Characteristic for deep partial-thickness burn wounds are thrombosed blood vessels that create ischemic area in which epidermal and dermal cells are forced to survive. These types of

wounds show an ambivalent clinical behavior with possibility of restitutio ad integrum on the one side and development into full thickness loss on the other side [15].

Recently, presence of apoptotic cells in the zone of stasis in burn wounds has been reported [6]. It is known that other ischemic events like undersupply of tissue oxygen in strokes, myocardial and renal infarctions show clinical and pathologic similarities to the zone of stasis in burns [16,17,18]. Typically in this context is the fact, that the anatomical viability is still present during the function is temporally inactive. A rapid revascularization of underperfused tissue areas is inevitable. Several studies showed that apoptotic cell death is involved in the biology of this intermediate zone [6,16-18]. Experimental interventions to inhibit apoptosis at appropriate time points during the cascade became a successful option in reducing the total infarct size following ischemia-reperfusion events in myocardium as well as brain [16,19].

In the past there have been no interventional studies to regulate apoptosis in deep partial thickness burn wounds. Previous interventions have only attempted to modulate the inflammatory response and ischemia that leads to necrosis in the zone of stasis [20,21]. This protective effect of the i-NOS inhibitor may be due to modification in NO induced vascular permeability. Additional to this theory, the inhibition of free oxygen radicals may play a significant role. The reduction of NO-release causes reduction of Peroxynitrite, which is produced in rapid reaction between NO and Superoxide. Peroxynitrite is known to be a toxic tissue destroying substance through increase of hyperpermeability [14]. Many cytotoxic actions of NO have been attributed to the chemical reactivity of Peroxynitrite (ONOO-) formed from NO by near diffusion-limited reaction with O2-. The reduction of Peroxynitrite can lead to stabilization of endothelial permeability and is therefore cytoprotective.

The excessive production of NO and therefore apoptosis is reduced with specific i-NOS-inhibitor. A nonspecific NO-synthase-inhibitor (Nomega-nitro-L-arginine, L-NNA) doesn't show a protective effect on burns [22]. Basaran et al. applied L-NNA in a caustic esophageal burn and they could show a significantly higher dead rate than in the group, where the specific i-NOS-inhibitor was used.

The therapeutic intervention may have clinical application for tissue preservation in the thermally injured wound. The study of exact mechanism of i-NOS inhibitor mediated protection is warranted. A "saving" of zone of stasis may reduce TBSA in burn injuries. Without any questions the clinical human application is still a challenge. Studies about potential side effects of long term application of selective i-NOS inhibitors are currently not available. The clinical application of i-NOS inhibitor in the first 24 h post burn appears reasonable, because our data show, the reduction of the apoptotic index is more pronounced at 24 h vs. 48 h.

Yoshimura [23], Sozumi [24], Lindblom [25] and others have administered NO inhibitors to various models of injury. Sozumi studied the kinetics and role of nitric oxide (NO) on vascular permeability using an ear thermal injury model. Vascular permeability was suppressed for 3 hours after a thermal injury by the preventive administration of nitric oxide synthase (NOS) inhibitors. The NO content in the injured region was significantly increased compared with the intact region. The plasma NO content was significantly increased in a biphasic pattern at 1 and 6 hours post injury. NOS inhibitors administered as therapeutic treatment suppressed vascular permeability 1 and 6 hours post burn.

In summary the apoptosis is a significant mode of cell-death in the zone of stasis in partial thickness burn wound and specific i-NOS inhibitor reduces this apoptotic injury.

Since costs in burn treatment constantly increasing, this progressive tissue loss may be additional load on health care. Other types of acute ischemic processes like strokes, myocardial and renal infarctions show clinical and pathologic similarities to the zone of stasis in burns [16-18].

Wound Healing Mechanisms after Burn Injury

The epidermis, because it is derived from ectoderm, is capable of regenerative healing. Deep dermal burns heal slowly, if at all, and depend to a large degree on the migration of keratinocytes from surrounding uninjured skin. This is also the mechanism whereby the interstices of meshed split-thickness skin grafts are filled in by keratinocytes that migrate from the skin bridges. The biology of epidermal renewal is currently an area of intense research. Translation into a useful technology that will improve wound healing and outcomes may soon be a reality [26].

Major burn injury is followed by an enormous inflammatory response. While it is transient systemically, burn wound may suffer from the effects of acute influx of inflammatory mediators and growth factors for a prolonged time. The burn wound contains a variety of cell types including platelets, neurophils, lymphocytes, macrophages, and fibroblasts, whose activity is regulated by a complex interplay of multiple cytokines as well as host neuroendocrine mechanisms. The principal molecular regulators controlling the evolution of the burn wound include vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF) and transforming growth factor-ß (TGF-ß). Transforming growth factor (TGF)-beta is essential for activation and proliferation of fibroblasts during the initial stage of wound healing. Sustained activity of TGF-beta is associated with hypertrophic scars and wound contraction leading to disfigurement and deformity [27]. In experimental models, use of neutralizing antibodies against TGF-beta has shown reduction in scar formation without adversely affecting wound healing [27]. New burn wound management strategies would involve reducing the extent of inflammatory response related to acute injury and regulating fibroblast-myofibroblast activity to reduce scarring and contracture without affecting wound healing and strength of wound repair.

Another recent study concluded that fibrocytes are present in abundance in acute burn wounds, and these cells appear to be involved in the local response to burn wound and may correlate with the later development of hypertrophic burn wound scarring. This might be very important in the future to predict those who will develop hypertrophic scar [28].

A potential promising new approach for wound healing and treatment involves the use of stem cells for skin regeneration. Investigators showed that collagen-glycosaminoglycan constructs seeded with mesenchymal stem cells improves healing and keratinisation, decreased wound contracture, and improves vascularisation. It may lead to the development of skin substitutes from the source of pleuripotent cells [29].

Agents, either systemic or topical applied are used to improve wound healing of burn wounds in several studies. The application of a novel nitric oxide (NO) containing topical gel improved re-epithelisation associated with increased abundance of fibroblasts and inflammatory cells [30].

Systemic Effects of Burns and Role of Apoptosis

The systemic pathophysiologic changes following thermal injuries associated with apoptosis affect multiple organs and body systems leading to clinical manifestations including shock, intestinal alterations, respiratory and renal failure, immunosuppression and others. Major thermal injury is associated with extreme hypermetabolism and catabolism beeing the principal metabolic manifestations after successful resuscitation from the shock phase of the burn injury. The metabolic response in burn patients is biphasic wherein the initial ebb phase is followed by a hypermetabolic and catabolic flow phase of injury [31]. The increased oxygen consumption/metabolic rate is in part fuelled by an evaporative heat loss from wounds of trauma victims, but likely also by a direct central effect of inflammation upon the hypothalamus [31]. Recent advances in the comprehension of underlying mechanisms of systemic complications have uncovered part of cellular and molecular processes, which are involved in triggering complication of thermal injuries.

Pathophysiologic changes that occur upon severe thermal injuries involve the cardiovascular system (myocardial depression, edema formation, hypovolemia), pulmonary (local vasoconstriction, edema), gastrointestinal (impairment of gastrointestinal motility and absorption, splancnic vasoconstriction, loss of mucosal barrier function with bacterial translocation, increased intragastric pH), hematopoietic (anemia, immunodepression) and renal (splancnic vasoconstriction). All these changes lead to important clinical syndromes such as shock, respiratory insufficiency and acute respiratory distress syndrome (ARDS), paralytic ileus, sepsis and renal failure. This complicated situation involves a variety of pathological events which will condition the clinical outcome of burned patients.

GUT/DIGESTIVE SYSTEM

The digestive system is impaired by neutrophil influx with extravasation in the lamina propria (postburn day 1), increased intestinal myeloperoxidase (postburn day 3), decreased epithelial cell proliferation, migration, and E-cadherin expression (postburn day 3), increased E. faecalis bacterial translocation (postburn day 3) [32] and massive apoptosis and moderate necrosis [33]. Such situation is dominated by two major events: first of all, by the oxidative stress secondary to hypoperfusion or delayed perfusion. Secondly, by TNF-alpha (α) production induced by macrophages primed by gamma delta (γδ) T cell after a thermal injury [34]. It is concluded that delayed resuscitation is responsible for mucosal apoptosis and that oxygen-free radicals generated during the process of ischemia-reperfusion injury also have a negative effect on mucosal cells [35]. Ischemia triggers oxidative stress leading to the generation of molecular mediators that ultimately will cause two types of cellular damage: necrosis and apoptosis. These molecular mediators consist of mucosal or monocyte-macrophage derived radical oxygen synthase (ROS) and NO synthase (NOS) activity that will lead to H_2O_2 and NO production, which are toxic to the enterocytes [36]. Inhibition of inducible NOS reduced the apoptotic rate in the gut. Also the changes in gut mucosal homeostasis after severe burn are affected by the activation of TNF- α-TNF receptor interaction [37]. γδ T cells were associated with increased TNF- α expression and gut epithelial turnover in the small bowel after severe burn [38].

Leukocytes and Lymphoid Organs

Thermal injury-associated specific immune deficiency occurs despite of indicators of systemic activation of the lymphoid compartment. Severely injured trauma patients usually experience T cell depletion but only a subset also develop T cell anergy [39]. Interestingly Leptin showed a positive protective effect against apoptosis [40]. Also a direct relationship between Nitric Oxide (NO) and apoptosis occurrence was demonstrated. NO had an influence on the synthesis of immunoregulatory and proinflammatory cytokines, such as interferon gamma (IFN-δ), interleukin-2 (IL-2), interleukin-6 (IL-6) and tumor necrosis factor (TNF) [41]. Another study demonstrated that NO produces cytostatic, apoptotic, and necrotic effects on activated T cells. Early immune suppression (3 days after burn injury) stimulates CD8(+) T cell late (14 d) hyperresponsiveness. These data could have broad clinical implications for allogenic skin grafting and rejection [42].

Heat shock proteins (HSPs) were reported to protect cells against a variety of environmental stresses. Major burns were shown to cause long-term, enhanced expression of HSPs in neutrophils along with increased oxidative activity and decelerated apoptosis. The enhanced expression of HSPs could regulate the oxidative stress response and the life-span of neutrophils in burn patients [43].

Morphologic changes were described in the spleen [44]. After 2 h from thermal injury numerous B lymphocytes accumulated in the markedly expanded marginal zone of the splenic white pulp. After 5 h B lymphocytes were present in the marginal zone as well as in the lymphoid sheath and follicles were markedly decreased in number with an increase of tingible bodies and tingible body macrophages. After 12 h the splenic white pulp became atrophic with the appearance of a small number of large blastic cells and mitotic figures. After 24 h the splenic white pulp was still atrophic with a decrease in the number of lymphocytes, especially B lymphocytes. After 48 h the lymph follicles were slightly enlarged and a small germinal centre occasionally appeared. A recovery in T cell number was observed only after 48 h. The percentage of CD4+ and CD8+ T cells in the spleen remained altered for 10 d after thermal injury [44].

Muscle

The skeletal muscle weakness that usually occurs after thermal injuries often causes hypoventilation and dependence on respirators, a condition that increases morbidity and mortality. Patients with severe burns [total body surface area (TBSA) of > 30 %)] had weaker muscle tonus even years after the trauma, suggesting either an inability to fully recover or an insufficient rehabilitation [45]. Morphologic changes present in muscles following distant thermal injuries include mitochondrial alterations [46] and intracellular lipid accumulation [47]. The endocrine status is also markedly altered with a sustained increase in proinflammatory “stress” hormones such as cortisol, other glucocorticoids and catecholamines by the adrenal medulla and cortex. These hormones exert a catabolic effect and the intensity depends upon the percentage of TBSA involved [48]. Furthermore, a variety of inflammatory circulating factors have been implicated including prostaglandins, IL-1, IL-6 and TNF-α [49,50,51,52]. Also the effect of surface cooling, which is frequently used after burn injuries to reduce tissue damage, on striated muscle and its apoptotic rate after thermal

burns was studied. It was concluded that the protective effect of surface cooling on traumatized tissues was due to an attenuation of the microvascular inflammatory response and associated response with an inhibition of the apoptosis process [53].

Liver

The liver furnishes the metabolic substrates to the organism it also mounts part of the inflammatory response. Studies have demonstrated that many of the metabolic perturbations of burns and sepsis may be due to inflammatory cytokines and these activate specific transcription of liver genes including classic acute phase response markers, complement, kinin, clotting, and fibrinolytic protein systems [54]. Hepatomegaly is a common finding at autopsy in severely burned patients. Large intrahepatocytic fat droplets within hepatocytes and cholestasis were important contributors to hepatomegaly. Other common histologic findings included congestion, centrilobular necrosis and cholestasis [55].

Heart

A depression of cardiac output immediately follows burn injury. As hypovolemia ensues, diminished plasma volume and reduced venous return then contribute to a continued cardiac output. However, even when plasma volumes are restored and both arterial pressure and urinary output are normalized, a persistent reduction in cardiac output remains. Many studies found that, during burn traumas, TNF-α, IL-1β, and IL-6 secretion are secreted by cardiomyocytes, and all these cytokines were correlated with an increased cardiac dysfunction [56,57,58]. Major burn injury also alters the flux of calcium ions between the sarcoplasmic reticulum and the cytoplasm [59]. Lipopolysaccharide (LPS) has been clearly demonstrated to induce cardiac apoptosis in many studies [60]. Endotoxin induces a TNF-α-dependent apoptotic cascade in the myocardium by caspases activation, which contributes to the development of cardiac dysfunction [61]. Furthermore, LPS is a potent inducer of inducible NO synthase (iNOS) in cardiac myocytes activating the apoptotic pathway [62].

Lungs

The lungs appear to be particular susceptible to edema formation, regardless of whether the burn injury is accompanied by an inhalation injury. Within the first 24 h after a severe burn, nearly all patients develop generalized edema which is related to the size of the burn and the timing, composition, and amount of fluid resuscitation [63]. Early after large burns there is a pronounced increase in pulmonary vascular resistence and pulmonary wedge pressures that derive from a general vasoconstriction of the microcirculation. Hypoproteinemia is also a main factor in the development of pulmonary edema [64]. In fact, this results from the loss of plasma proteins from the burn wound and the intravenous infusion of large volumes of crystalloids fluids during the first hours of resuscitation. In addition to reducing plasma oncotic pressure, hypoproteinemia appears to alter the intestinal matrix in a way that facilitates the movement of fluid across the capillary endothelium [65].

The physiologic consequences of such injuries include impaired gas exchange and reduced airway compliance. Furthermore, the morbidity of severe cutanous burn injuries is increased when accompanied by smoke inhalation, a stimulus for the inflammatory response and ARDS [66]. Histologic alterations of lungs in burns injury include intestinal edema, hyaline membrane formation, and neutrophils sequestration within the lung [67]. The increase in pulmonary microvascular permeability is probably mediated by neutrophils activations and TNF-α production [68]. Complement, neutrophils, and oxygen-derived free radicals all appear to be intimately involved in the pathogenesis of burn-induced acute lung injury. Complement activation generates the potent anaphylatoxin C5a, resulting in neutrophil superoxide and hydrogen peroxide release, enhanced chemotaxis, and neutrophil-endothelial cell adherence [69]. The lung is also an important source of TNF-α release after severe burns. TNF- α, IL-6 and IL-8 are present within the bronchoalveolar lavage fluid of patients 48 h after burns and probably contribute to the increased microvasculature permeability [70].

Future Perspectives

Extended burn injuries cause systemic modification of the patient's clinical conditions that usually worsen the prognosis. Hypovolemia, respiratory insufficiency, shock are only a few of such changes. The pathophysiologic mechanisms that underlie them are complex and involve almost all organs and body systems. Apoptotic processes following burn injury have been described increasingly. Future potential therapeutic targets which need to be addressed is the clinical significance of this systemic phenomenon and development of promising anti-apoptotic drugs with the intriguing possibility to block the "systemic apoptotic response" and its pathophysiologic effects. For instance, specific therapies could derive from the experimental application of selective antiapoptotic drugs i.e. selective inhibitors of death receptors, caspases or the proteasome complex.

Another potential pathway of new therapeutic options after thermal injuries is gene expression profiling, which has inspired new hope for finding genes involved in complications resulting from burn injury. Therefore, genetic dissection of burn injury should be carried out in a global context. A similar investigative approach is the understanding of Pseudomonas aeruginosa burn wound infections by profiling gene expression. Pseudomonas represents a key opportunistic pathogen causing severe acute and chronic nosocomial infections. It is prevalent in burn wounds and generally multi-drug resistant. Understanding the genetic programs underlying infection is essential to develop highly needed new strategies for prevention and therapy. Future efforts should focus on the identification of direct virulent factors and elucidation of their mode of action. These new data sets obtained from global transcriptional profiling could be essential for the development of new targets and options for prevention and intervention of burn wound infections.

In summary in the last decade major effort is made to establish new strategies to improve clinical outcome of burned patients. In our opinion the key points of future research should be infection control, especially against multi-resistent bacteria, new wound healing pathways, intervention of apoptosis and genetic dissection of the burn injury.

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Chapter 5

BURNS DURING ARTHROSCOPY DUE TO USE OF ELECTROSURGICAL DEVICES: PREVENTION, CAUSES, AND TREATMENT

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ABSTRACT

There were thousands of arthroscopic procedures performed in the United States each year. Roughly 85% of all surgical procedures will employ some type of electrocautery. Burns and other thermal injuries, from direct electrocautery and arthroscopic devices, can create lifelong morbidity and even mortality.

The components of electrocautery are the power generator, a handheld monopolar or bipolar electrode, and, if necessary, a patient return electrode. Heat generation is dependent upon several factors, including type and duration of the current, type of tissue, tissue cross section, humidity of the skin, and more.

In monopolar electrocautery, the current, which has entered through a single, small-surface-area point, must be dissipated and complete the circuit through a patient return electrode (PRE). The current, which entered the body though the small surface area electrode, exits through a large surface area pad. Safety guidelines regarding skin temperature are built into some electrocautery devices.

"Aberrant grounding" can occur with a wide variety of operating room materials as well. These are unexpected areas of low or high resistance which influence the direction of current and can be a risk factor for burns.

Arthroscopic fluid is an essential part of arthroscopic surgery; it creates a working space and functions to flush debris and blood from the operative field. Case reports are emerging regarding the significant intra-articular temperatures these fluids can reach with use of electrocautery.The amount of flow during arthroscopy is important to heat regulation, with low-flow states reaching higher temperatures and taking longer to cool than high-flow states. Arthroscopic light sources have been shown to cause cutaneous burns, and have started fires when placed on drapes.

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The most important factors to prevent burns using electrocautery are the surgeons themselves. Inspecting the patient for sources of impedance, medical history, body hair, scars and implants should all be considered. The grounding pad, if necessary, should be kept cool and placed on a clean, dry, hairless area. Power settings and alarms should all be preset before beginning a case.

Local wound care has been shown effective in many burns associated with electrocautery. Antibiotic ointments and sterile dressings are often all that is necessary to resolve these burns. For deeper burns, it is reasonable to obtain a plastic surgery consultation, even intra-operatively. Rarely, surgical intervention has been necessary to resolve these issues, including skin grafts and muscle flaps.

INTRODUCTION

There were thousands of arthroscopic procedures performed in the United States in 2010. Year after year, this surgical technique is becoming more popular. It has risen in popularity because it is minimally invasive, requires less dissection, and can have shorter recovery times. One of the aspects of arthroscopy which can be underappreciated, both in its benefit and risk, is electrocautery [2, 5-12]. Although it is a powerful and versatile surgical tool, it carries a unique subset of complications.

ELECTROCAUTERY BASICS

Electrocautery has been a staple in operating rooms since the time of Cushing and Bovie [13]. Roughly 85% of all surgical procedures will employ some type of electrocautery, also known as radiofrequency energy (RFE) [14]. Electrocautery in arthroscopy works under the same basic principles as in traditional, open procedures. The components of electrocautery are the power generator, a handheld monopolar or bipolar electrode, and, if necessary, a patient return electrode.

The surgeon can determine many of the parameters under which the machine operates. A high frequency electrical current of 0.4-3 megahertz enters the body though a small-surface-area electrode. It is important to stay within this range, as unwanted effects for frequencies outside of these parameters have been shown to occur. For instance, a radiofrequency of 300 kilohertz or less can create muscle fasciculations and is therefore avoided [12, 15]. Power is another function which is controlled, though it must be limited to 150 Watts in children and 400 Watts in adults [7].

The electrical current generated by the machine creates heat, which coagulates or cuts tissues which the electrode is on or near. Heat is generated according to the equation $\Delta t = (\text{amperage}^2/\text{area}^2) \times \text{time} = (\text{amp}^2/\pi r^2) \times \text{time}$ [16]. Heat generation is dependent upon several factors, including type and duration of the current, type of tissue, tissue cross section, and humidity of the skin, among others (See Table 1). As it enters the body, this current can generate temperatures of over 1000 degrees Celsius [7, 10]. However, this extreme temperature is quickly dissipated, to such a dramatic extent that tissues just one centimeter from the contact point will rise only one degree C [10].

Table 1. Factors which affect heat generation at the operative site and at the patient return electrode

Factors of Heat Generation at Operative Site	Relative Effect on Heat Generation
Increased Current	↑↑↑
Longer activation time	↑↑↑
Longer time spent in one place	↑↑
Decreasing electrode tip size	↑
Increasing electrode tip size	↓
Blood / Coagulum at surgeon electrode	↓↓
Factors that Influence Heat Generation at Return Electrode	Relative Effect on Heat Generation
Decreasing water content in pad	↑↑↑
Decreasing size of pad	↑↑↑
Hair	↑
Scar	↑
Increased fat content	↑
Decrease distance between electrode and pad	↑
Aberrant grounding / Capacitative coupling*	↓*
Increasing size of pad	↓↓

This table gives selected examples of different conditions and their relative effect on heat generation at the operative site. The arrows indicate relative increased risk of local heat generation (↑) or decreased (↓) risk. The number of arrows signifies the magnitude of influence. The asterix (*) indicates that heat generation at the return electrode is decreased, however, increased at the area of aberrant grounding.

An important component of this discussion is electrical "impedance." Impedance is resistance to flowing current. Higher impedance will slow electrical current, and low impedance will allow faster transmission. Areas of high impedance can cause the current to flow in aberrant and sometimes dangerous directions. It can occur at any place in the circuit: coagulated blood at the surgeon's electrode, the patient's body itself, and at the patient return electrode [1]. Impedance during surgery usually averages between 2,000-3,000 ohms [7].

MONOPOLAR AND BIPOLAR ELECTROCAUTERY DEVICES

Monopolar electrocautery devices employ a handheld electrode that transmits current through a single point; this current then travels through the patient to a patient return electrode distant to the operative site (Figure 1a). Patient return electrodes will be discussed later in this chapter. The temperature is generated dependent on the function to which the device is set, as well as the length of time it is functioning.

Most monopolar devices have "cut," "coagulation," and "blended" current options. These settings refer to the machines "on" time. "On" time is defined as the percentage of time the electrocautery device is in use with current running through the tip. For instance, in the "coagulation" function, there is a 6% "on" time, and a 94% "off" for the duration that the machine is activated but no current is running through the tip. During the more intense "cut"

function, the current is “on” 100% of the time. With this function, the target tissue cells will actually be vaporized and there is little or no coagulation or thermal damage to the cells [17]. There is a third function, called “blended cut” which is a form of “cut” featuring pauses in the “on” time, allowing for tissue coagulation between bursts of cutting [18]. The more current that goes through the tissue, the higher the temperature will be. Monopolar devices can be temperature and power controlled for patient safety [12].

Bipolar electrocautery is different from monopolar in that the current is transmitted between the tines of the device, which is shaped like a forceps (Figure 1b). The device’s conduction path is within an irrigation fluid which is expressed when the device is activated. The effects of this device are secondary to the thermal and ionic modification of the tissue. The tissue grasped between the tines receives the current, decreasing the power requirements and increasing the specificity and accuracy of the electrocautery [19]. Bipolar electrocautery also will not spark, giving the surgeon greater control over the operative conditions [19].

There is a role for both modalities in the operating room, as there are advantages and disadvantages to each. For example, bipolar electrocautery doesn’t require the use of patient return electrodes, whereas a monopolar device cannot function without it. Bipolar devices are also power controlled, meaning they deliver a constant power output while activated [12]. By way of comparison, monopolar devices are temperature controlled, meaning they have a regulator which automatically can adjust power output to maintain a selected temperature.

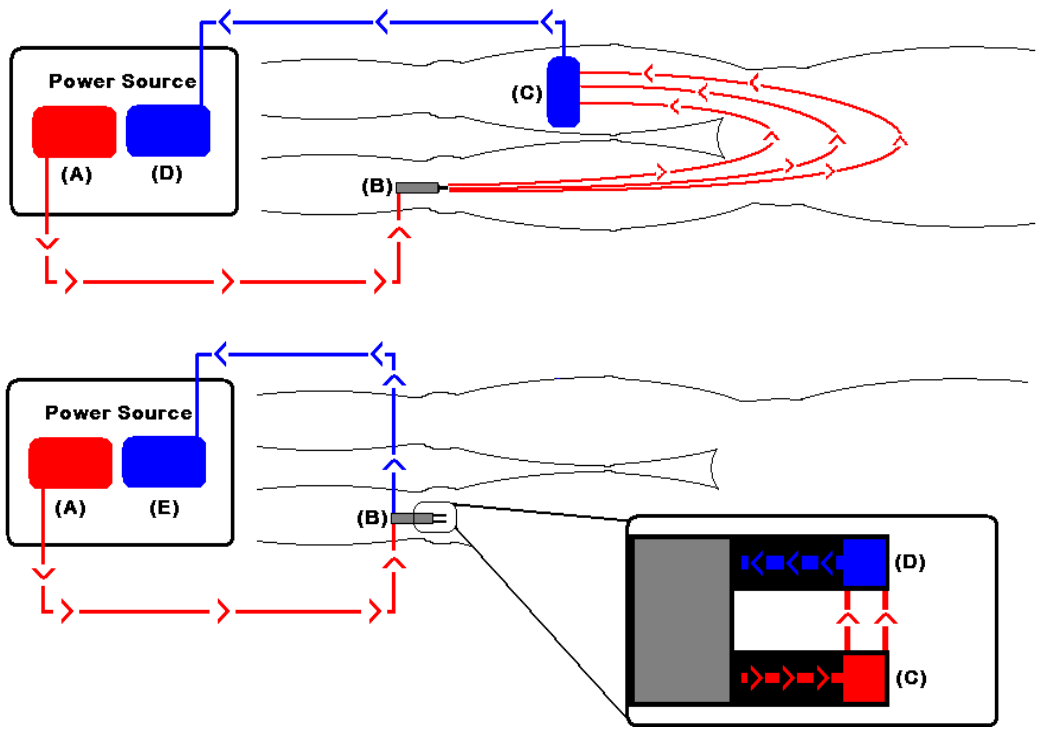

Figure 1a. Monopolar electrocautery. In this figure, power is generated by a power source (A) and travels to the tip of the surgeon’s electrode (B). The current then passes through the patient’s body (thin red lines), exits via the patient return electrode (C) and returns to the generator (D). Figure 1b. demonstrates bipolar electrocautery, where current flows from the generator (A) to the surgeon’s electrode. It then passes between the electrode tips (C and D, inset picture), which are holding tissue. Current then returns directly back to the power source (E).

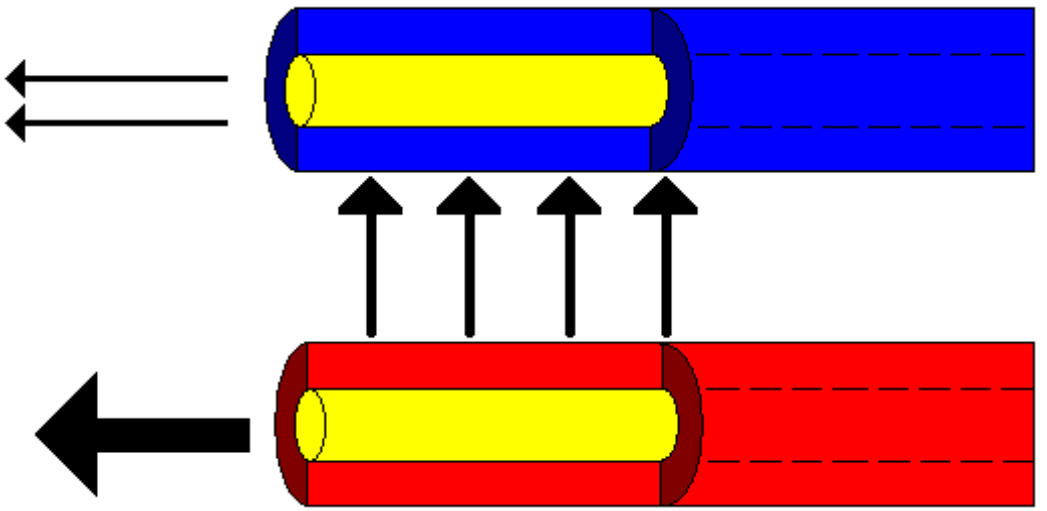

Figure 2a. Capacitative coupling: current running through the insulated red wire affects the inactivated insulated blue wire, causing current to flow through that wire (small black arrows). The close proximity of these two wires increases the risk of coupling. The greater the distance between the two conductors the less likely this is to happen. For this reason, it is a good idea to avoid clipping wires next to each other in the operating room. Of note, if there is tissue between the wires when coupling occurs, a burn is possible.

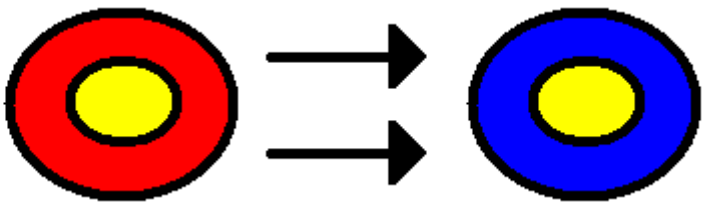

Figure 2b. Head-on view of the coupling described in figure 2a.

These regulators can adjust power as rapidly as 50 times per second [20]. In certain settings, power controlled bipolar electrocautery has been shown to cause more cell necrosis than temperature controlled monopolar [21, 22].

Bipolar electrocautery also has a low voltage waveform than monopolar, which decreases the chances of capacitative coupling as well. This is a condition whereby "electrical current is transferred from a conductor (electrode) through intact insulation into adjacent conductive materials such as other instruments, cannulas, or patient tissue (See Figure 2) [19]." Imagine two wires separated by rubber insulation with current flowing through one wire. Coupling would occur if current leaked to the second wire. The magnitude of current is dependent on proximity and surface area of the conductors' interface, insulator, voltage, and frequency of the current [9]. In a more practical sense, think of the wires surgeons often clip together on the operating field to keep them organized.

To minimize dangers from capacitative coupling, it is suggested to use the lowest effective voltage, check all wiring for cracks, holster any instruments not in use, and employ the use of an active electrode monitor [9]. An electrode monitor is a device, available for

bipolar and monopolar electrodes, which monitor the units' power output and resistance. If the machine is operating suboptimally or malfunctions, an alarm will sound. These alarms can be adjusted by the operator and can greatly enhance patient safety.

Patient Return Electrode

In monopolar electrocautery, the current, which has entered through a single, small-surface-area point, must complete the circuit and be dissipated through a large surface area pad known as a patient return electrode (PRE). By using a large pad, an equal amount of current can be removed from the body but with far less heat and therefore less cellular damage. Although these pads are made to uniformly take up current from the body, orientation, body location, and chemical composition will change their efficiency.

The PRE has taken many forms throughout history, varying in composition and size. A few examples of past electrodes include: metal plates, cardboard plates, cardboard with aluminum sheeting, dry adhesives, and hydrophilic conductive adhesive electrodes [1]. PREs continued to evolve through the 1980s with the use of a flexible electrode covered in an adhesive gel. This helped to ensure a good, uniform, fixation to the body [11, 23]. These pads are made of at least 50 percent deionized water, contain polyvinylpyrrolidone (PVP) and are designed to uniformly adhere to the skin [11]. Occasionally, nursing staff will warm these pads for patient comfort, which can dry the pad. In a case report by Sanders et. al., a dessicated PRE gel pad was implicated in a third degree burn at the electrode site [6].

PREs account for 70% of the injuries in electrocautery, making it especially important to check all components of the PRE prior to use [15]. Regardless of which dispersive pad is used, the potential for burns at any point of concentrated current should always be a concern [11]. If the temperature at the PRE site exceeds 112° Fahrenheit (44.4° C), a burn may occur [1]. Safety guidelines regarding skin temperature are built into some electrocautery devices. Per the International Electrotechnical Commission, the maximum allowed temperature is 45° C for 100 minutes. With normal resting skin temperature between 29-33° C, the maximum safe rise in skin temperature when using a device is 6° C. Any more than 12° C will cause burns [24].

A maximum safe power density of approximately 1.5W/cm^2 must also be maintained [16]. For example, a maximum power output of 200W and a minimum surface area of 133cm^2 [16]. Regardless of the size of pad used, a large, uniform surface connected at all points to the patient is essential. Most single pads range from 60cm^2 up to 180cm^2 [7]. Much larger pads are available; these can be upwards of a 720 square inch pad placed under the patient, separated from them by an impermeable drape and sheet. This is referred to as a "non-contact plate." The large surface area compensates for the larger impedance of the impermeable drape and pad. This pad has been shown in evidence based and anecdotal literature to have good results with no reported complications [8, 13]. Typically, PREs are sized by the age of the patient, for example, infant, child, or adult.

Even if the PRE has a very large surface area, the current will always follow the path of least resistance to the edge closest to the operative site. This point where current first encounters the PRE is known as the "leading edge". This is the case because, by design, the PRE has a lower resistance than the human body and the leading edge of the pad will provide

a lower resistance path for the current relative to the patient tissues. With this in mind, the side with the longest edge should be facing the operative site [16].

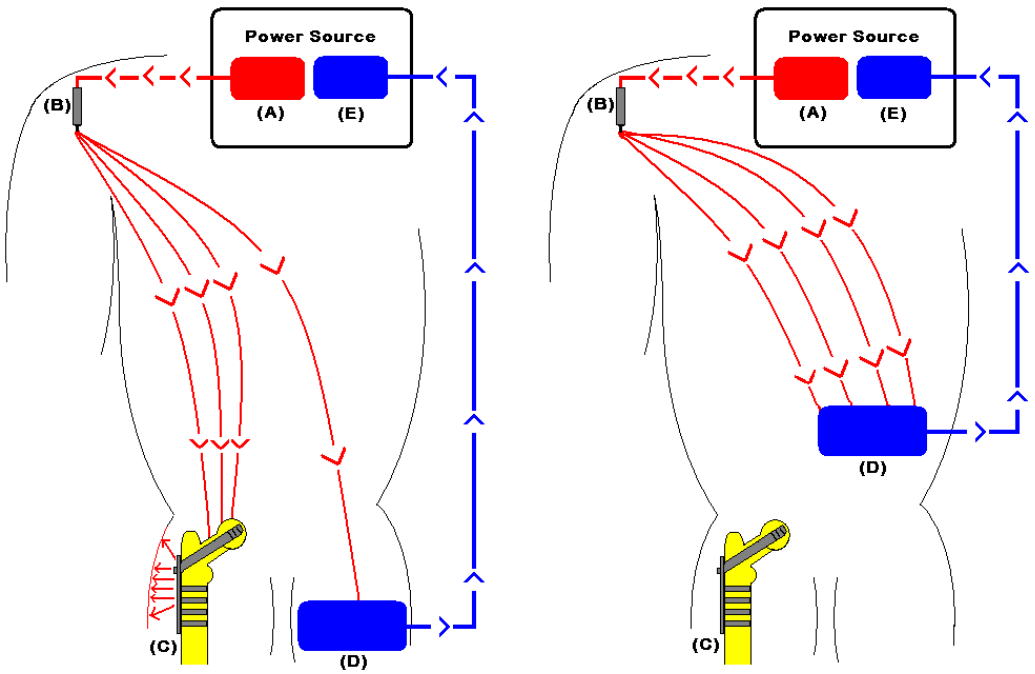

Figure 3a. Aberrant grounding. In this figure, current from the generator (A) is transferred from the surgeon's electrode (B) to the patient's body. However, the lower resistance of the orthopaedic implant (C) draws current away from the patient return electrode (D). Instead, it is dissipated at the patients' skin, causing a burn. Figure 3b. This is an example of how to avoid the aberrant conduction from figure 3a, a safer position for the PRE is diagramed, and conduction of electrical current is free to return to the power generator (E) without complication.

"Aberrant grounding" can occur with a wide variety of operating room materials (Figures 3a and 3b). These are unexpected areas of lower or higher resistance which influence the direction of current. These can be in the form of electrocardiographic leads, temperature probes, insulated surgical table contacts, arterial lines, motor-evoked potential monitoring electrodes, and electroencephalogram electrodes [2]. Monitoring these areas is the responsibility of all operating room staff. Likewise, it is important to inspect electrical cord insulation, as cracks in insulation have been known to cause burns [9].

Finally, the location of the PRE is important as well. The closer the PRE is to the surgeon's electrode, the more current can easily flow through the body [5]. Typically, it is suggested that the PRE be placed away from bony prominences, conducting implants, and scars [16]. It should, however, be placed as close to the operative site as is safe, in order to limit the chances of a short circuit [25]. Another consideration is the concomitant use of monopolar and bipolar electrocautery. In this situation, a PRE is placed on the patient and can theoretically attract current from a bipolar device if the two are close enough. However, in most practical cases there is a low likelihood of this happening, as often the PRE is distant enough from the operative field to be safe [19].

ARTHROSCOPIC IRRIGATION

Arthroscopic fluid is an essential part of arthroscopic surgery; it creates a working space and functions to flush debris and blood from the operative field. This fluid is often comprised of normal saline or lactated ringers, and can be heated to room temperature prior to infusion. The fluid itself has been shown to have the least amount of damage to the articular cartilage when heated to 37° C prior to infusion into the joint when compared with 4°C and 25°C [26]. However, there are no nationally recognized guidelines regarding the temperature of arthroscopic irrigation fluid [4]. Case reports are emerging regarding the significant intra-articular temperatures these fluids can reach [3, 4]. Another major concern is leakage of hot arthroscopic fluids.

The amount of flow during arthroscopy is also very important to heat regulation. During electrocautery, irrigation fluid temperatures have been shown to reach greater than 80°C after two minutes in a no-flow setting [27]. Good et. al performed a comparison of intra-articular temperatures during arthroscopy in 100% flow, 50% flow, and no-flow settings. The investigators measured the effects of continuous use for one minute, or intermittent. They found that the average maximum temperatures were 32.5°C ± 14.95°C in the 100% flow setting, 37.4°C ± 16.82°C in the 50% flow, and 85°C ± 20.21°C in no flow settings. In this same trial, the investigators looked at how long it took the fluid to cool to safe levels (defined as less than 45°C). In 100% flow, 8±4.21 seconds were required, 50% flow required 16±10.75 seconds, and no-flow required 125±49.5 seconds to cool [28]. Clearly there is a dramatic change in fluid temperatures depending on flow rate, with less heating and faster cooling [27-29]. It is generally accepted amongst arthroscopists that high flow rates are beneficial and necessary.

As we stated earlier, arthroscopic fluid is often pre-heated in a warming cabinet prior to infusion. In one case study from Huang et. al. of a knee arthroscopy, the temperature of this fluid was noted intraoperatively to be extremely warm because of a malfunctioning heating cabinet and the problem rectified immediately. The case was completed and the patient appeared to have no adverse effect from the fluid. Unfortunately, over the course of the next several days, blisters developed in the lines of fluid runoff, which ultimately presented as full thickness burns. More importantly, the knee, which required repeat arthroscopy for suspected infection, had become fibrosed with poor range of motion. Ultimately, after a prolonged course requiring several procedures, the knee went on to arthrodesis (See figure 4). The burns required a lateral gastrocnemius muscle flap and split-thickness skin graft [4]. The complication in this case was extreme; however it illustrates the important point of checking the irrigation fluid prior to infusion.

In a case report by Kouk et. al, the heated arthroscopic fluid from use of electrocautery for extended periods during subacromial decompression and bursectomy caused severe burns across the patient's chest and arm. In this case, limitations in the suction device led to suboptimal performance, and electrocautery was performed for two minutes with heated fluid running over the patient. This ended only after extensive redness and blistering were noted intraoperatively. The patient was treated with local wound care, consisting of antimicrobial ointment and silver sulfadiazine ointments, after 7 months the patient had remnant scarring from the burns (See figure 5) [27].

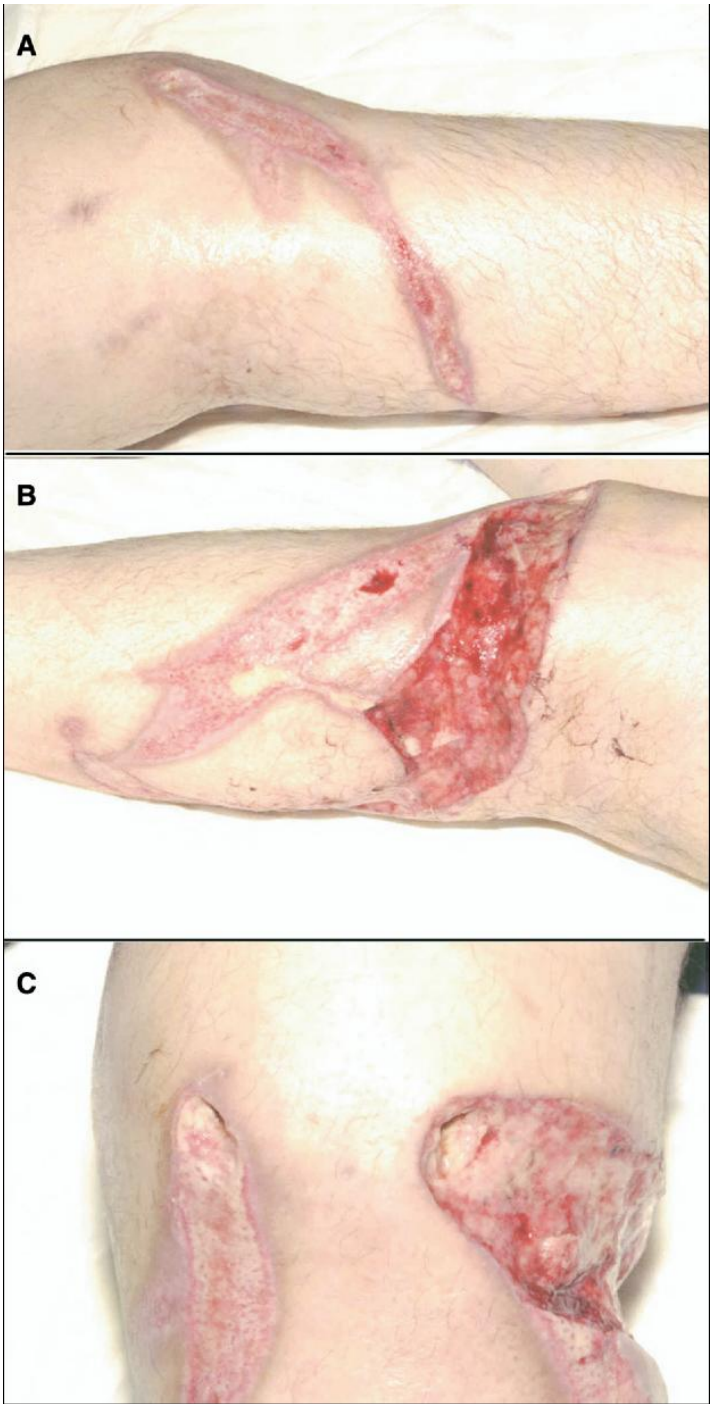

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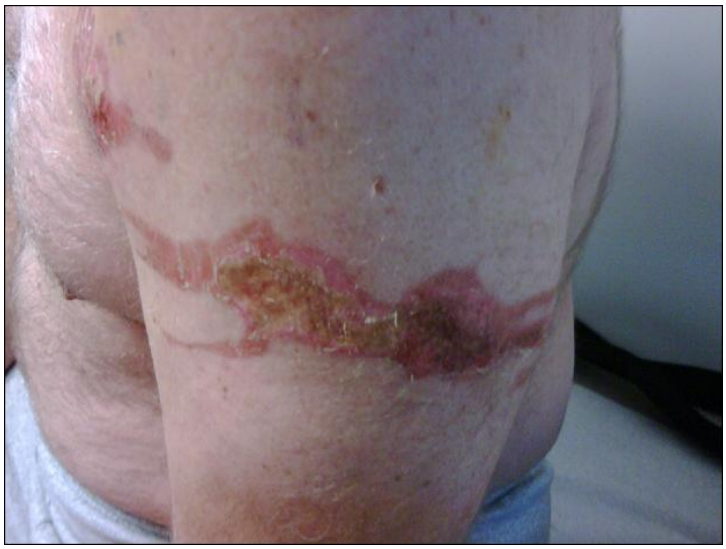
Figure 4a-c. Clinical pictures of a left knee after hot arthroscopic fluid was found to be draining. The fluid was accidentally overheated prior to infusion. This patient went on to knee fusion secondary to superinfection and arthrofibrosis.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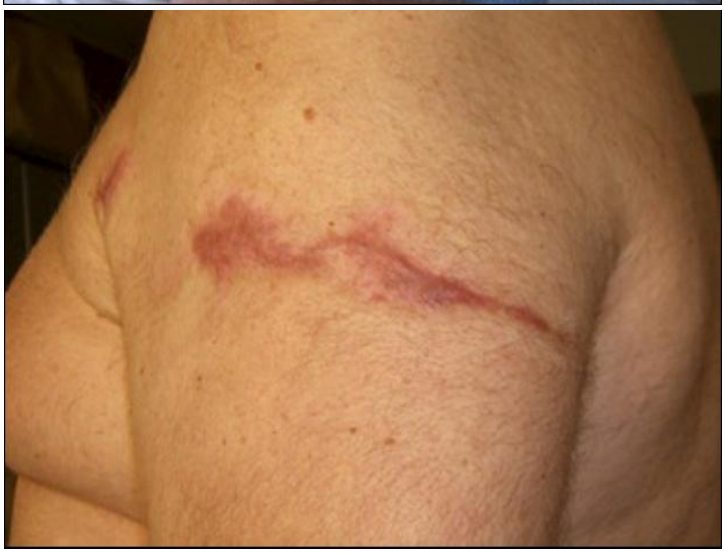
b.

Reproduced with permission from Kouk et. al.

Figure 5a. Superficial burns from hot arthroscopic fluid which ran off along the lines of gravity. Figure 5b. is the same patient after months of healing, the wounds became relatively asymptomatic except for occasional itching.

These reports are used to illustrate that arthroscopic fluid should be carefully managed, both prior to infusion and intraoperatively. The surgeon should advise the operating room staff to check all arthroscopic fluids prior to infusion. The ideal rate of infusion is dependent on many factors, including which joint is being operated on, what procedure is being performed, and if electrocautery is actively being performed. Although one should use the appropriate flow for the location and procedure, a high flow rate, approaching the maximum allowable rate, should be used during electrocautery. The surgeon or their assistant should intermittently feel the effluent to protect the patient against thermal injury as well. In addition, all operating room staff should be cognizant of the patient's skin color and condition and bring any change to attention.

RISK FACTORS

All of the aforementioned components of arthroscopic electrocautery have the potential to cause intra-operative complications. In this section, both patient and operating room factors are described in detail.

Patient Factors

The body itself is an integral part of the electrocautery circuit. Body composition, size, and distance that the current has to flow through all change the characteristics of electrocautery (See table 2).

Table 2. This table highlights certain patient factors which can influence the risk of burns and what can be done to prevent them

Patient Factors	Effect on Risk for Burns	Suggested Prevention
Presence of implant	↑↑	Place return electrode away from implants, check areas of known implants for changes, use bipolar when possible
Vascular compromise	↑	Choose return electrode in area of better blood flow
Hypothermia / Vasoconstriction	↑	Maintain adequate patient temperatures
Hair at electrode site	↑	Shave hair if present
Oil / Lotion on skin at electrode site	↑	Wash with non-alcoholic cleanser
Jewelry	(↔)↑	Remove all jewelry or isolate with gauze and tape
Increased muscle content	↓↓	Place return electrode on muscular area

The direction of the arrow indicates increased risk of burn (↑), decreased risk of burn (↓), or no effect on burns (↔).

Body hair has high impedance and can also disrupt the ability of a PRE to maintain contact, altering the characteristics of current outflow. Certain sites of a PRE can be more closely attached to the skin, letting current flow preferentially through a smaller area, creating more dermal heating, and potentially more irritation and burns. It is important to shave any area that will be involved in the circuit, ensuring uniform contact between the body and PRE.

Skin moisture, either with body oils or lotions, as well as overly dry skin can lead to danger areas for burns. It is important to wash and dry skin when indicated to maintain a uniform conducting surface [25].

As blood flow is essential to dissipating heat from electrocautery, it is important to assess the patients' vascular status prior to electrode placement. In the presence of peripheral vascular disease, vasoconstriction (including hypothermia), or obstruction to blood flow, caution must be taken to limit electrocautery and allow for adequate temperature dispersal [16].

Electricity will flow more effectively through muscle than fat. Muscle is higher in vascularity than adipose and therefore a better conductor of current [18]. There are two considerations for the surgeon regarding muscle content. First, obese patients may require a higher power setting to create the same therapeutic effect. Second, this changes where the ideal location of a PRE. The general rule is to place the electrocautery pad as closely as safely reasonable to the operative site [18]. Typically, the outside of the thigh or a muscular abdomen is the recommended position for a PRE.

Implants of any kind alter the body composition and can create "aberrant grounding" which was discussed briefly in the section on patient return electrodes. As current will preferentially flow through areas of least resistance, metal implants of any kind can create a short-circuit in the electrocautery system and be a source of burns. Electrical current can flow preferentially through the highly conductive materials and concentrate the current in the surrounding tissues. Several reports of orthopaedic and neurosurgical implants causing severe burns in patients have been reported [2, 7, 30].

To prevent aberrant grounding in the patient with implants, it is recommended to use isolated electrosurgical units, avoid or minimize contact between patient and instruments, and avoid excessive activation of the electrocautery device, and place the PRE well away from any implants [2].

If the patient has a pacemaker or implanted defibrillator, bipolar electrocautery is recommended, but if monopolar is necessary, place the PRE so that current will flow away from the implant [25].

Operating Room Factors

The various types of equipment in the operating suite are all potential areas of danger during electrocautery. Important factors are the function and shape of the electrode, the grounding pad, other medical devices in the vicinity which may be broken or misplaced, pooled fluids, and surgeon technique.

Newer models of power generators have monitors that constantly check the condition of the patient-PRE interface. These monitors will alarm if there is a significant change in the status of this circuit [23]. Some power generators will monitor the resistance in ohms, and if the resistance becomes too little or too high, will automatically shut down the system. Other, more adaptive systems will take an initial reading and allow only a 40% change in resistance from that original value [1, 5].

Another source of complications with the use of electrocautery stems from the electrocautery wiring itself. We have already discussed in detail the many types of instruments which can be sources of burns during arthroscopy. Regardless, constant vigilance should be the standard. Vilos et. al. describe a large (5x1 cm) third degree burn during a procedure requiring both monopolar and bipolar electrocautery. In their investigation as to the cause of the burn, they noted the insulating wire to the bipolar electrode was damaged and because of the arrangement for dispersive electrodes, a short circuit to the patient's body occurred (See figure 6) [9]. Although this is a unique example, it is clear that inspecting all electrosurgical equipment prior to use is essential. To avoid a short circuit when using both modalities, it is possible to disconnect one while the other is in use, this would guarantee that no current could deviate from its intended course. This may be impractical in a busy operating

room, therefore, avoid multiple cords attached together to drapes, if foot pedals are used be sure to know which pedal controls which device to avoid activating the incorrect one [9].

Arthroscopic light sources have anecdotally been shown to cause cutaneous burns. They have been shown to create enough heat to start fires when placed on drapes. Investigations into the arthroscopic tip indicated maximum temperatures of 41.9°C to 95°C in air, and 22.1°C in water. Placed against disposable drapes, they can cause charring with no perforation [31, 32]. The light cable tip, however, can rise to temperatures between 101°C and 177°C, which quickly start fires and cause burns [31, 33]. It is recommended to put light sources on standby mode immediately after extraction from the joint to avoid these complications.

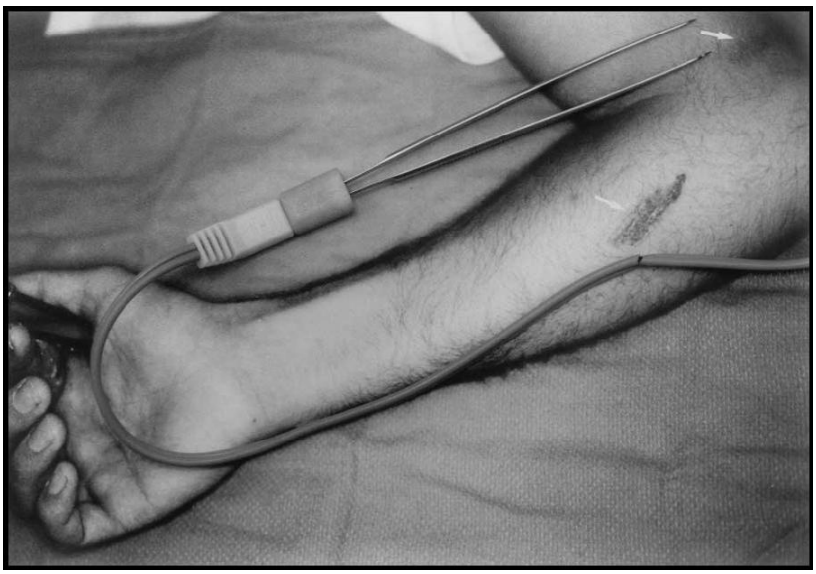

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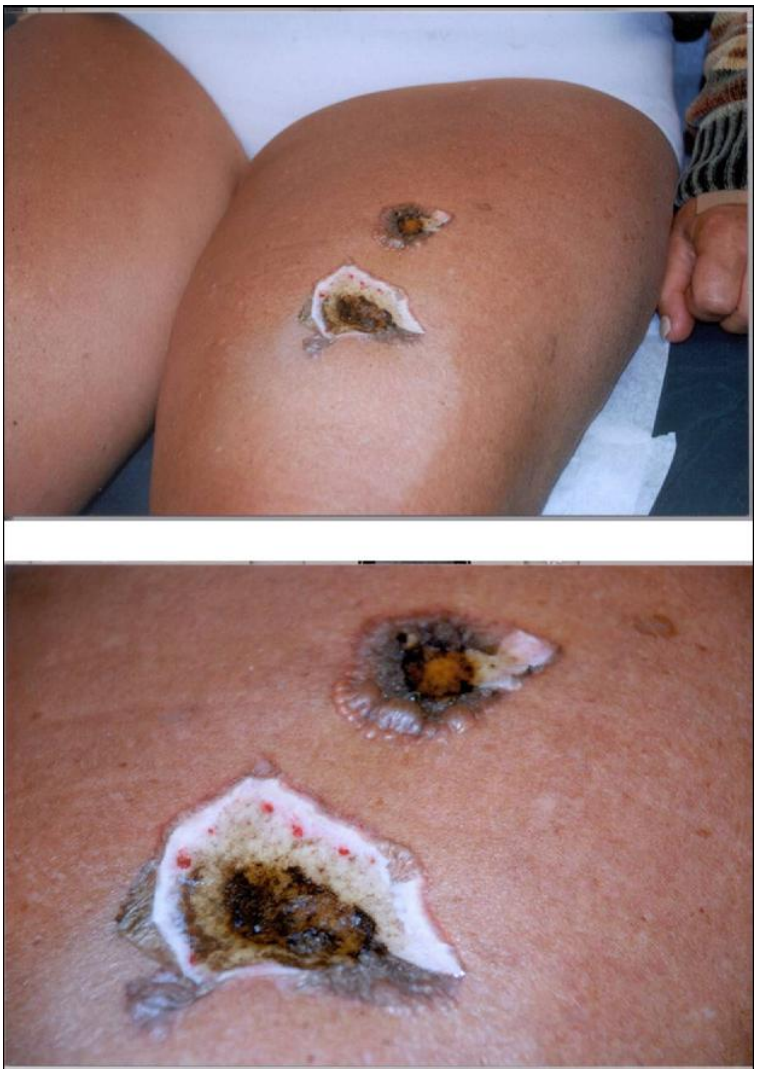
Figure 6. Burns on the forearm of a patient secondary to a crack in the insulation of a radiofrequency device.

Pooled fluids can also be a danger in the operating room. Regardless of which electrocautery device the surgeon is using, activation can heat any pooled fluid. Heating can lead to extreme temperatures and third degree burns have been reported [30]. This should serve as a warning to keep a clean surgical field with proper placement of surgical equipment.

The most important factor that can contribute to burns using electrocautery are the surgeons themselves. Zinder and Parker state that “Ignorance is the leading cause of these injuries in the operating theater [5].” They emphasize that electrocautery, although basic in its physics, has the potential to do great harm in the hands of someone who does not appreciate the many subtleties of this tool.

A common mistake, especially among less experienced surgeons, is the ineffective use of the electrode tip. In principle, the smaller the area the current travels, the faster and hotter it will become. With this in mind, the smaller the tip, the more effective the electrocautery will be. It then follows that using the broad edge of an electrode will produce less heat, requiring more “on” time and higher power settings, raising the risk of thermal injury to surrounding tissues [18].



Reproduced with permission from Sanders et. al.

Figure 7. The thigh of a patient whose patient return electrode dessicated, which created a point of increased current. These burns healed with superficial wound care over the next several months.

Leaving the electrode tip in one location for too long will increase the "thermal spread" (heat travelling to the surrounding tissues). To prevent this, electrocautery production companies recommend a "rest period" defined as the use of a 30 second break for every 10 seconds of electrocautery. The purpose of this pause is to allow the surrounding tissues at the operative site and grounding site to cool [23].

It is important to realize that, although preoperative planning is essential, conditions can change quickly in the operating room. For instance, if the electrocautery device appears to be working less efficiently, consider that there may be a serious cause for this dysfunction. In an illustrative case of oral surgery by Zinder and Parker, a bipolar electrocautery device was noticed to be working less effectively, requiring increased power output from the machine. It was discovered a full thickness burn was present at the patient's right oral commissure. They postulated that the bipolar tongs were accidentally held against the commissure, causing a

short circuit. In the operating room, this was interpreted as inefficiency by the machine and power was increased. In reality, the bipolar was sending a significant current through the commissure, resulting in this burn. With this in mind, it is important to maintain direct contact between the electrode and the operative site, only. Also, keep in mind that if something appears to be working incorrectly, explore the problem rather than considering it machine dysfunction.

Table 3. Recommendations for Nursing Staff to Prevent PRE Lesions

Use full surface adhesive patient return electrodes and contact quality monitoring systems
Inspect the return electrode package when opening. Do not use PRE if package is damaged or outdated.
Inspect pad and cable for defects. Check for adequate hydration of the adhesive and gel.
Do not warm the gelled patient return electrode.
Choose the appropriate sized PRE for each patient and follow manufacturer's recommendation regarding power restrictions on smaller PREs.
Choose a muscular site close to the surgical site for pad application.
Avoid degreasers, prepping agents, and pooling of fluids.
Clean and and/or safe as recommended by PRE manufacturer instructions for use
Avoid close contact with warming blanket.
Use firm application technique. Check entire PRE and edges for full contact with patient
Do not place safety straps over PRE. Avoid other pressures including patient or staff person's body weight.
Check PRE whenever patient is re-positioned or if there is any tension on the cable.
Do not re-apply a patient return electrode that has become detached.
Always use the lowest power settings that provide the desired surgical effect.
Check PRE prior to increasing normal power settings.
Remove PRE slowly, supporting patient's skin during removal.
Refer to the PRE and ESU manufacturer for complete instructions for use, cautions and warnings.

Fickling and Loeffler. *Patient Return Electrode Lesions.* Information Hotline News. Vol. 5. Issue. 3. September, 2003.

In many of the case reports of burns during arthroscopy, when a piece of equipment was not functioning as expected, or the patient showed signs of burn, the problem was immediately addressed (See figure 7). Further damage was prevented by alert surgeons and their staff. Their knowledge of electrocautery principles and good clinical judgment helped prevent more catastrophic injury to the patient.

Prevention

Awareness of potential complications and proper preoperative planning will help surgeons effectively minimize patient morbidity and mortality (See table 3).

Inspecting the patient for sources of impedance, medical history, body hair, scars and implants should all be considered. Jewelry has been a source of debate, and isolated generators limit the danger from them. However, it is recommended that all jewelry be taken off prior to surgery. If the jewelry cannot be removed, it is suggested the item be covered with gauze and taped into place [34]. Rings and bracelets can constrict if the limb swells during surgery, thereby increasing the contact area for current to flow [34].

The PRE is an important factor in burns during electrocautery and care should be taken to minimize risk during surgery. The electrode must be stored in a cool place, and inspected for damage or dessication, prior to placement on the patient. Also, check for the expiration date prior to placement.

The PRE site must be inspected prior to use. Remember to keep a clean, dry, hairless area which is free of any oils or lotions. If scrubbing is necessary, remember to avoid alcohol scrubs and make sure any combustible cleaning materials are evaporated prior to PRE placement. Be aware of previous surgeries and avoid areas where the patient has any implants. Keep the PRE away from areas of scar or bony prominences. Inspect the electrode after placement for folds or air bubbles which can increase the risk of burn.

Location and orientation of the PRE are important considerations as well. Place the PRE in an area of higher muscle content away from the operative field, like the abdomen or lateral thigh. Remember to keep the longest edge of the PRE facing the operative site to avoid a "leading edge" burn.

Power settings and alarms should all be preset before beginning a case. Remember that monopolar devices can be temperature controlled, and if there is an active electrode monitoring system, make sure that it is activated and the alarms are audible.

Make sure that the anesthesiology team and nursing staff are aware that any object in contact with the patient carries the potential to cause a burn. Intermittent checks of EKG leads, endotracheal tubes, arterial lines are recommended.

As described earlier, arthroscopic fluid can pose a significant risk to patients. Intraoperatively, warmed arthroscopic fluids should be checked for excessive temperatures. Scheduled inspections of any heating cabinet should also be employed. The surgeon should ask an assistant to intermittently check arthroscopic fluid effluent for dangerous temperatures, as well as exposed skin for unexpected changes. All flow and suction devices should be checked and functioning optimally. Light sources should be placed on standby mode as soon as possible to decrease their potential for fire or burns. Remember that, although the camera tip may not cause burns, uncovered light sources can start fires quickly.

The surgical field should be kept clean, dry, and clear of extraneous wires or unused instruments. Any unused devices or instrumentation must be holstered or returned to the technician.

Electrocautery should be used with proper technique, using the lowest effective setting, and minimizing time of activation.

As always, full manufacturer recommendations should always be followed for all devices; some of the prevention instructions have been listed in table 1. Finally, awareness of changing conditions in the operating room should be fully explored, as they can herald serious problems.

Treatment

Burns secondary to electrocautery or arthroscopic fluid should never be taken lightly. Although most reports of these burns have had complete resolution with local care, more catastrophic outcomes can occur. Although rare, deaths secondary to superinfection of these burns have been reported [10].

If a burn has occurred, it is important to recognize the problem as soon as possible. Depending on the extent of the burn, they can be difficult to spot in the early stages. First degree burns present as reddening of the affected area, second degree burns can show blisters, edema, and hyperemia, a third degree burn can present with destruction of the skin, with eschar formation, fourth degree burns present as damage into the deeper tissues such as muscle or bone.

There are different types of PRE burns that have been described. For instance, one burn type is a small to medium burn, dime or half dollar in size, presenting as a second or third degree burn. This may be identical to a portion of the PREs perimeter, and there may be a charred section of tissue near the edge or the adhesive surface, indicating arcing between skin and PRE. The cross section of the burn can be dish shaped [11]. A second type of burn arises from lower energy, but longer exposure. This will usually present as a first or second degree burn, will mirror the size and shape of the PRE, and may take days to weeks to present [11].

Local wound care has been shown effective in many burns associated with electrocautery. Antibiotic ointments and sterile dressings are often all that is necessary to resolve these burns. For deeper burns, it is reasonable to obtain a plastic surgery consultation, even intra-operatively. Rarely, surgical intervention has been necessary to resolve these issues, including skin grafts and muscle flaps.

CONCLUSION

Thermal injury during arthroscopy can take many forms, and is caused by many factors. Understanding the basic principles of electrocautery in the setting of arthroscopy is essential to prevention of these complications. While severe complications do occur, they are rare and often avoidable. The most effective way to manage burns is with early recognition, local wound care, and consulting the appropriate service if necessary.

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Chapter 6

THE PATHOPHYSIOLOGY OF BURNS

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ABSTRACT

This chapter provides an overview of the body's local and consecutive, systemic pathophysiological reaction to a thermal lesion. In addition to immunological processes at the cellular level, the development of systemic inflammatory response syndrome (SIRS) is also explained within the scope of the pathophysiological reaction to the burn injury. Building on this, the two current theories (the "two-hit model" and the model of posttraumatic immunosuppression) on how multiple organ failure develops will also be discussed. The resulting pathophysiological responses to the burn trauma by the individual vital organs will be explained. In addition, this chapter will also discuss the options presently available to treat organ failure.

THE PATHOPHYSIOLOGY OF BURNS

A burn trauma is not just an injury to the skin. In fact, it presents the treating physician with a variety of problems which can manifest themselves in each of the body's organs. The survival rate of patients with major burn injuries has been optimized due to being able to better control the events of shock, thanks to modern intensive care including the related use of high-tech medicine, as a result of providing early operative treatment to the burned body surface, and thanks to the possibilities offered by modern plastic surgery. Despite this fact, multiple organ failure still represents the most frequent cause of death in burn victims as a result of extensive burn injuries. In order to provide adequate treatment, one must first understand the pathophysiological processes which occur when the body is in shock. This chapter will provide an overview of the pathophysiological reaction to the burn injury and its effects on the entire body.

DEVELOPMENT OF BURN WOUNDS AND LOCAL REACTION

Burn wounds are caused by exposure to open flames, contact with hot surfaces or gases, as a result of electrical shocks or injuries from electric arcs, by radiation, and as a result of scald injuries from hot liquids. In this context, the extent of the injury caused by the burn depends on its temperature and the length of exposure. Temperatures of 40 - 45°C can already lead to protein degradation and intracellular enzyme dysfunction when exposure time is over one hour. Above a temperature of 45°C, the cells ability to compensate is completely exhausted, and continued exposure can lead to cell destruction with subsequent tissue necrosis. If the temperature continues to increase, the initial degradation of cellular proteins will evolve into definitive protein denaturation, which leads to a defined coagulative necrosis. The result is the destruction of the proteins and a change in the protein structure, which leads to protein rearrangement and cell fragments, which have toxic, antigenic, and immunomodulatory effects [1]. Knowledge of these processes is required before one can understand the model first described by Jackson regarding the various zones of damage within a burn wound [2]. Jackson divided the burn wound into three zones, in which case the core, i.e. the location of the actual thermal injury, is described as the zone of coagulation. Surrounding the coagulation zone is what's known as the zone of stasis. The zone of stasis contains cells whose function has been damaged, but due to the lower temperatures found in this surrounding area, are not destroyed. Depending on the injury, tissue in the zone of stasis exhibits limited capillary perfusion with an overall reduction in blood flow. Cells in the zone of stasis whose function is already damaged at the time of the acute thermal injury can also become necrotic and subsequently die as a result of the body's own reaction to the injury (releasing mediators, immunomodulators). This is referred to as the "deepening of the burn wound." Simultaneously, a local reduction in perfusion as well as ischemia with destruction of cell function occurs. The release of highly potent vasoactive mediators results from a cascade reaction between the microvascular endothelium and the polymorphonuclear leukocytes, which has an effect on circulation throughout the entire body. According to Jackson's shell model, the outermost of the three zones is called the zone of hyperemia. This area has not been directly affected by the thermal injury and exhibits vasodilation or hyperemia on the surface of the skin as a reaction to the processes occurring within the burn wound. Understanding the pathophysiological processes which occur in the three zones described by Jackson as a reaction to the thermal injury is a crucial aspect of the treatment principles described below. In order to ensure that the thermal injury is limited locally to the actual location of destruction in the zone of coagulation, further injury in the zone of stasis must be prevented at all costs. In addition to mechanical pressure, hypothermia, and hypovolemia due to circulatory depression with the resulting lack of tissue perfusion, in particular infection represents a further cause of progressive necrosis. These pathophysiological processes within the burn wound can lead to the zone of stasis transforming into a necrotic area. Toxins, cell fragments, and bacterial metabolites can cause microthromboses in the capillaries surrounding the wound with successive hypoxemia, consecutively leading to the death of the remaining vital cells in the zone of stasis and subsequent tissue necrosis. In this way, these pathophysiological processes which occur as a reaction to the burn wound can transform a superficial burn into a deep burn which must be operated on [3].

In the pathophysiology of a burn wound, massive soft tissue edema represents an additional problem for the cell's oxygen supply. As a result of the increase in pressure, it leads to tissue compression which restricts the supply of oxygen and nutrients to the cells in the zone of stasis which remain vital. Capillary circulation ceases above a mechanical pressure of 32 mmHg. The edema as a reaction to thermal injury occurs as a result of a change in hydrostatic pressure in the capillaries, a shift in interstitial fluid, the change in colloid osmotic pressure in blood plasma, and a shift in the capillary filtration coefficient. An edema forms as a result of this imbalance between the increased volume of interstitial fluid compared to lymph drainage. As such, one finds a large amount of plasma proteins in the burn wound's lymph fluid. Due to the additional increase in vascular permeability, these plasma proteins are discharged into the interstitial fluid. These proteins foster the burn edema by means of the increased colloid osmotic pressure in the interstitial fluid caused by the influx of water. This entire process is referred to as a capillary leak. The cause of the increased permeability of the capillary walls for the proteins is the direct damage to the endothelium as a result of the thermal injury in the area of the burn wound. In the pathophysiology of a capillary leak, on the one hand direct mechanical damage to the cell wall due to the pressure of the edema is assumed, however this is also attributed to the release of mediators such as histamine, bradykinin, and oxygen radicals at the cellular level [4]. A systemic inflammatory reaction in the body occurs as a response to the thermal injury, with the following processes:

- Activation of the coagulation cascade
- Activation of the complement system
- Thrombocyte activation and aggregation
- Direct and indirect endothelial damage
- Granulocyte migration and activation
- Macrophage migration
- immunomodulation with interleukins

IMMUNOLOGICAL EFFECTS AS A REACTION TO THE BURN

Thanks to advancements such as the creation of special burn centers, balanced fluid therapy, early enteral nutrition, and most recently, the ability to cover the burn area of skin with cultivated autologous keratinocytes, lethality has been able to be reduced to approx. 15%, with multiple organ failure representing the most common cause of death. From an etiological perspective, a dysregulated immune system exists as the body's reaction to the burn within the scope of multiple organ failure. Initially, an inflammatory focus exists, which is present in the form of the wound area after the thermal injury. The systemic inflammatory response syndrome (SIRS) which occurs as a result of immunosuppression, colonization of the burned body surface, and translocation from the intestine to the bloodstream is defined as the systemic response to the invasion by microorganisms. These include gram-positive and pram-negative bacteria, viruses, and fungi. The same systemic reactions can also occur without the bacterial exposure in cases with massive trauma or extensive burn necrosis.

Signs of Incipient SIRS

- Hypertonia or hypotonia
- Hyperthermia or hypothermia
- Hyperventilation or hypoventilation
- Intestinal atony with ileus
- Oliguria and a general increase in all retention values
- Disorientation and clouded awareness
- Leukocytosis or leukopenia, CRP increase

From Systemic Inflammatory Response Syndrome (SIRS) to Multiple Organ Failure

SIRS is a trauma-related systemic inflammatory reaction. SIRS is defined by the presence of at least two of the following symptoms:

- Pulse ≥ 90 beats/min
- Breathing rate ≥ 20/min or $PaCO_2 \leq 32$ mmHg
- Body temperature ≥ 38° C or ≤ 36 ° C
- Number of leukocytes ≥ 12,000 or ≤ 4000/µl

The cell damage present in all burn victims plays a central role and is a precondition in the pathophysiology of the inflammation and the development of SIRS. The burn injury's wound areas bring about a vicious circle, in which damage to the parenchyma of the organ due to local inflammation results from the excessive pathophysiological reaction with capillary leakage and the development of edemas. Over the course of this local inflammatory reaction, the effector cells express an increasing number of receptors, so that as the length of the inflammation increases7 the responsiveness and extent of the inflammatory reaction progresses. The transition from SIRS to multiple organ failure is seamless. The mechanisms for the transition from SIRS to multiple organ failure are unclear; at the present time two hypotheses exist regarding the development of sepsis, the two-hit model and the model of post-traumatic immunosuppression [5]. In addition, a number of studies have been conducted which lead to the assumption that the two are not at odds, but in fact a chronological sequence of events.

Two-Hit Model

As a result of the actual burn injury (the first hit), the immune system has already been placed in a state of increased activity, and the inflammatory responses to damages such as operative trauma, hypotension, and wound infection represent an additional powerful stimulus. The effect of endotoxins (lipopolysaccharides) from gram-negative bacterial walls as the second hit has been verified in experiments (two-hit model of immunosuppression).

Because of these doses of endotoxins, the macrophages are completely activated and produce TNF-α. This mechanism leads to extensive organ dysfunction and even irreversible organ damage. The cause is ultimately the insufficient microvascular oxygen supply and the resulting tissue hypoxia. Studies have shown that the combined administration of small doses of endotoxin and TNF-α triggered extensive hypotension and excessive metabolic effects similar to administering a high dose of one of the individual noxa [6]. Endotoxin from microorganisms still induced many of the symptoms associated with SIRS such as fever, hypotension, activation of the complement cascade, the coagulation cascade, and the release of platelet-activating factor [7].

MODEL OF POST-TRAUMATIC IMMUNOSUPPRESSION

After the initial stimulation of the immune system as a result of the burn, counterregulatory immunosuppression occurs as time progresses. As a result of the thermal injury, burn victims exhibit extensive t-cell suppression, while b-cell proliferation is only affected slightly. In addition, the antibodies in the early stages of the humoral immune response (HIR), IgM, and in the later stages, IgG are all affected. Both lymphocyte proliferation as well as antibody synthesis no longer function correctly, and dissociations occur in the immune system's signal transduction system. Not only does the reduced formation of regulatory factors in the immune system contribute to misregulation, but the increasing number of components which have formed do as well. An increase in immunosuppressive mediators such as IL10 and prostaglandin PgE2 was also detected [8]. Although the local and physiologically controlled humoral and cellular immune defense is sensible and necessary when fighting infection, an excessive immune reaction promotes the development of SIRS and the resulting development of organ damage:

ORGAN DAMAGE WITHIN THE SCOPE OF SIRS

Multiple organ failure is comprised of a combination of cardiovascular, respiratory, renal, hepatic, gastrointestinal, and lastly, neurological failures. Etiologically, a generalized malfunction exists induced by an inflammatory chain reaction which is caused by the release of mediators (TNF, interleukines) from macrophages, lymphocytes, and endothelial cells. While initially the prognosis is determined by the burn wound with its large wound areas, later it is dominated by hypermetabolism triggered by SIRS, with its increased microvascular permeability and impact on individual organs. This is why prevention and treatment of multiple organ failure are dependent on correcting tissue perfusion as early as possible. The temporary replacement of limited organ functions (respiration, hemofiltration) represents the treatment method of choice. The elimination and/or antagonization of immunomodulating mediators is currently the topic of extensive basic research. Current treatment methods are limited to the early excision of the burn wound, influencing the cardiopulmonary system, limiting the increase in retention values, early enteral nutrition, and widespread antibiotic screening [9].

EARLY EXCISION OF THE NECROTIC TISSUE

The main benefit of rapidly excising the burned necrotic tissue is that it shortens the period of time in which the patient is exposed to the risk of an invasive wound infection [10,11]. The release of inflammatory cytokines when removing burned necrotic tissue is possible; however the incidence of bacteremia after surgical excision is insignificant [12]. The severely burned patient only benefits from the complete removal of necrotic tissue, however, as leaving inflammatory regions supports pathological inflammatory reactions [13,14].

CARDIOVASCULAR FAILURE

When the effects of insufficient volume appear, myocardial depression occurs, and free radicals are viewed as the cause of myocyte membrane damage. A combination therapy comprised of free radical scavengers with adequate volume therapy (Parkland formula) leads to an improvement in left-ventricular contractility [15]. In addition, within SIRS the exorbitant release of mediators has a cardiodepressive effect. The insufficient reaction of myocardial contractility to beta-adrenergic substances which can be observed within the scope of SIRS is triggered by the inducible NO synthase in cardiac myocytes which is stimulated by mediators and cytokines [16]. The following is a list of the primary goals in the treatment of sepsis-induced cardiovascular depression [17]:

- Increase cardio output
- Lower peripheral resistance
- Normalize heart rate
- Increase tissue perfusion
- Reduce the arteriovenous difference

RESPIRATORY FAILURE

Inhalation injury represents the trauma most often associated with a lethal outcome beyond that stemming from the actual burn wound. Only in a small number of cases does the initial x-ray of the lungs correlate with the extent of the organ damage caused by the inhalation injury [18]. In the event of cell destruction with the associated stimulation and migration of alveolar macrophages, chemotactic factors are released which cause a massive recruitment of leukocytes in the lungs. The inflammatory reaction of the lung parenchyma can be attributed to an activation of leukocyctes and the subsequent release of mediators, proteolytic enzymes, and the formation of free oxygen radicals. These enzymes and free radicals destroy the mucosa and increase capillary perfusion, and subsequent capillary leakage occurs. The interstitial lung edema which develops as a result causes fluid sequestration in the alveolar space to occur. A vicious circle results from the formation of hyaline membranes which then causes exudate to form, with the result being that the

pulmonary gas exchange becomes continuously worse. The lung parenchyma which has already been damaged in this way represents the ideal breeding ground for opportunistic pathogens, which ultimately cause pneumonia.

Noncardiac pulmonary edema → Reduced compliance → Formation of hyaline membranes → Development of arteriovenous shunts → ARDS → Lung failure

Respiratory failure within the scope of SIRS, usually occurring through the stage of tachypnea and hypercapnia, is an indication for intubation and respiration. By controlling breathing it prevents increased respiratory work; the supply of O2 increases and ventilation of dependent sections improves. Acute respiratory distress syndrome (ARDS) represents a form of lung failure with edema formation which results from the loss of the alveolocapillary membrane. Due to the negative effect of mediators on Type II pneumocytes, surfactant deficiency and the associated alveolar collapse with atelectasis development occurs. These pathological changes can be prevented by keeping the alveoli open using positive end-expiratory pressure (PEEP). In addition, periodically changing the patient's position in their Stryker bed can also improve oxygenation.

RENAL FAILURE

Acute kidney injury (AKI) is a constellation with an unfavorable prognosis, since it is associated with a high level of lethality. It either originates within the scope of an acute trauma as a complication of insufficient volume or occurs later within the scope of sepsis. The established dialysis and filtration methods offer sufficient opportunities for mechanical organ replacement and prevention of an increase in retention values. Popular methods include hemofiltration and hemodialysis, as they allow volume to be controlled adequately, although bleeding complications have been observed more often. The function of the kidneys is stressed as a result of low intravascular pressure, low oncotic pressure, in certain conditions due to protein loss, and consequently, due to the increased accumulation of substances normally excreted in the urine. Urine production of at least 50 ml/h is considered a parameter for sufficient renal function in severely burned patients. In the first few days after a burn injury, renal function can be limited. Since flushing out the burn edema beginning on the second day post-trauma is desirable, the use of diuretics may become necessary to maintain the body's water balance.

LIVER FAILURE

The pre-existing condition of reduced liver function (hepatitis, fatty liver, cirrhosis) often seen in the population of burn victims can lead to an acute decompensation as a result of hypoxic and septic factors. In this context, a reduction in hepatic blood flow must be judged particularly critically. If the gall bladder becomes involved in the form of cholecystitis, the indication for a cholecystectomy must be applied quite liberally.

INTRA-ABDOMINAL COMPARTMENT SYNDROME

The abdomen is considered, similar to the extremities or the skull, to be its own compartment, in which the anatomical structures located within can expand up to a critical limit without the function of the organs being affected. If the pressure in this closed space is so high, however, that sufficient perfusion to maintain the function of the organs is no longer possible, one speaks of abdominal compartment syndrome. In contrast to pregnancy, the rapid, acute increase in pressure must be viewed critically. Burch's trio, comprised of hypothermia, coagulopathy, and therapy-refractory metabolic acidosis, is postulated to be a pathophysiological correlate and predispose patients to intra-abdominal compartment syndrome [19]. A reduction in mesenterial blood flow can already be observed at a pressure of 10 mmHg, which results in a reduction in perfusion of the intestinal mucosa [20]. As intra-abdominal pressure increases, the thin-walled mesenterial veins become compressed, which results in an increase in the mucosa edema which already exists at this time. The result is ischemia and the danger of the loss of the mucosal barrier, which would foster bacterial translocation. The loss of this barrier can also trigger sepsis. Measuring intra-abdominal pressure is easy and carried out in a non-invasive manner transvesically using an inserted transurethral or suprapubic bladder catheter. The trend in the absolute values should be evaluated. Surgical decompression of the abdomen can be indicated in the event of impending abdominal compartment syndrome. From a pathophysiological perspective, bacterial translocation is the subject of fierce debate, since from a pathological and morphological perspective, initially no evidence of a primary intestinal lesion exists. On the other hand, it is considered agreed that mucosal lesions represent a sufficient weakening of the intestinal barrier compared to endogenous bacteria of the intestinal flora [21]. The results of experiments with animals have shown that certain types of intestinal bacteria do transcend the mucosal barrier and relocate in other organ systems [22]. Whether or not the results of these animal experiments can be applied to humans remains debatable [23]. Additional attention should also be turned to the development of pseudomembranous colitis as the result of the usually long-term antibiotic treatments. Since the burn injury results in an inflammatory reaction in all organ systems, including the intestinal tract with edema, atony, and paralysis, enteral feeding through a stomach tube must begin as early as six hours post-trauma. The goal here is to maintain the function of the gastrointestinal tract and prevent parambulating peritonitis caused by gastrointestinal stasis [24, 25]. Beginning with 25 ml/h, the amount administered is increased up to 100 ml/h on the third day and then maintained. Caloric intake of 2500-3000 Kcal should be calculated and provided for depending on the patient's individual size, original weight, and age. To prevent intestinal villus atrophy, 50 mg of glutathione is mixed in with the enteral nutrition formula. In addition to enteral feeding, one must also ensure that evacuation of the bowels is well-regulated. In general, this should be supported pharmaceutically by administering propulsin, lactulose, and/or SAB Simplex upon beginning with nutrition through the feeding tube. Sphincter extension, cleansing enemas, and colon massages can also serve as additional measures within the scope of burn treatment and intestinal atony caused by medications. If the aforementioned measures are not successful, parasympathomimetic drugs (neostigmine) may need to be administered intravenously.

SURGICAL TREATMENT

Burned necrotic tissue should be removed as quickly as possible in order to deprive microorganisms of a nutrient medium for an infection and to minimize an excessive immune response. Jancekovicz's introduction of early necrosectomy into the treatment protocol for severely burned patients in 1970 represents a significant milestone in burn treatment [26]. In addition to immediate necrosectomy directly after the thermal injury (within 24 hours post-trauma), which for the most part is no longer carried out in many centers due to the increased intraoperative lethality, early necrosectomy of the burned tissue (within 72 hours post-trauma) represents the most common method used today. An additional benefit is that the burn edema subsides within the first three days. Within a week to ten days after the thermal injury, necrosectomy should be carried out on the lion's share of the burned skin. An early surgical excision of the necrosis has proven to be beneficial, even if these procedures are associated with in some cases severe blood loss [27]. The main benefit of the early excision of burned necrotic tissue is that it shortens the period of time in which the patient is exposed to the risk of an invasive wound infection [28,29]. The release of inflammatory cytokines when removing burned necrotic tissue is possible; however the incidence of bacteremia after surgical excision is insignificant [30]. The burn victim only benefits from the complete removal of necrotic tissue, however; leaving inflammatory regions supports pathological inflammatory reactions [31].

SUMMARY

Above a temperature of 45°C, the cells ability to compensate is completely exhausted, and continued thermal exposure leads to cell destruction with subsequent tissue necrosis. The result is the destruction of the proteins and a change in the protein structure, which leads to protein rearrangement and cell fragments, which have toxic, antigenic, and immunomodulatory effects. Simultaneously, a local reduction in perfusion as well as ischemia with destruction of cell function occurs. The release of highly potent vasoactive mediators results from a cascade reaction between the microvascular endothelium and the polymorphonuclear leukocytes, and this has an effect on circulation throughout the entire body. Due to the additional increase in vascular permeability, a discharge of plasma proteins into the interstitium occurs. These proteins foster the burn edema by means of the increased colloid osmotic pressure in the interstitial fluid caused by the influx of water. This entire process is referred to as a capillary leak. The cell damage present in all burn victims plays a central role and is a precondition in the pathophysiology of the inflammation and the development of systemic inflammatory response syndrome (SIRS). The burn injury's wound areas bring about a vicious circle, in which damage to the parenchyma of the organ due to local inflammation results from the excessive pathophysiological reaction with capillary leakage and the development of edemas. Beyond a certain burned area, multiple organ failure occurs, and from an etiological perspective in this case a generalized malfunction exists induced by an inflammatory chain reaction which is caused by the release of mediators (TNF, interleukines) from macrophages, lymphocytes, and endothelial cells. While initially the prognosis is determined by the burn wound with its large wound areas, later it is dominated

by hypermetabolism triggered by SIRS, with its increased microvascular permeability and impact on individual organs. Cardiovascular, respiratory, and renal failure are the most common types of organ failure which occur within the scope of multiple organ failure. Early surgical excision represents the most important treatment method for burn injuries. The burn victim only benefits from the complete removal of necrotic tissue, however; leaving inflammatory regions supports pathological inflammatory reactions.

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Chapter 7

THE BURN RECONSTRUCTIVE UNITS ON THE FACE AND NECK

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ABSTRACT

The concept of aesthetic units and subunits has not always been considered in functional reconstruction of the face and neck in extensively burned patients, since prevention of scar contracture and functional reconstruction are foremost considerations. Here, we review previous works in this field and revisit the concept of "aesthetic units" and "aesthetic subunits". We advocate the novel concept of "burn reconstructive units," which have been categorized into ten units: 1. forehead unit, 2. nasal unit, 3. eyelid unit, 4. cheek unit, 5. upper lip unit, 6. lower lip unit, 7. mental unit, 8. auricular unit, 9. nape unit, and 10. anterior neck unit. "Burn reconstructive units" are designed to prevent and release scar contracture in addition to improving the aesthetics of the wound, and are thus considered as "functional units" in contrast to "aesthetic units." It is considered that burn reconstructive surgeons must strive to achieve both functional and aesthetic reconstruction, and should consider various options on a case by case basis.

INTRODUCTION

The concept of "aesthetic units" was first reported by Gonzales-Ulloa 1-4). He believed that superior surgical results can be obtained in complex facial reconstruction by replacing lost skin with grafts or flaps of similar histology, thickness, and texture 5). Subsequently, the concept of "aesthetic subunits" was reported by many authors 6-9). Generally, aesthetic subunits are employed with three guidelines 10): 1. if a defect is larger than 50% of a subunit,

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enlarge the defect to incorporate the entire subunit, 2. use an undamaged contralateral subunit as a reconstructive model, 3. devide large defects into multiple defects.

The concept of aesthetic units and subunits is quite useful for aesthetic reconstruction of the face and neck. However, in our experiences, the units have not been always useful for functional reconstruction of the face and neck, especially in extensively burned patients. In these cases, prevention of scar contracture and functional reconstruction are of paramount importance. Specifically, the selection of reconstructive methods and the shape of skin grafts and flaps to prevent contracture are important. Thus, we advocate the novel concept of "burn reconstructive units" in addition to aesthetic units and subunits for face and neck reconstruction, especially in extensively burned patients.

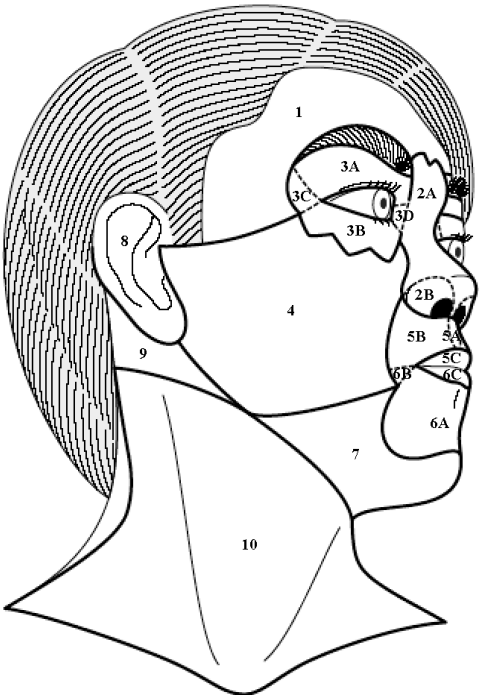
THE CONCEPT OF "BURN RECONSTRUCTIVE UNITS"

Face and neck "burn reconstructive units" are illustrated in Figure 1. The reconstructive units were developed based on the original aesthetic units 2), but have been modified according to our experience in preventing scar contracture after reconstruction using skin graft or flap transfer.

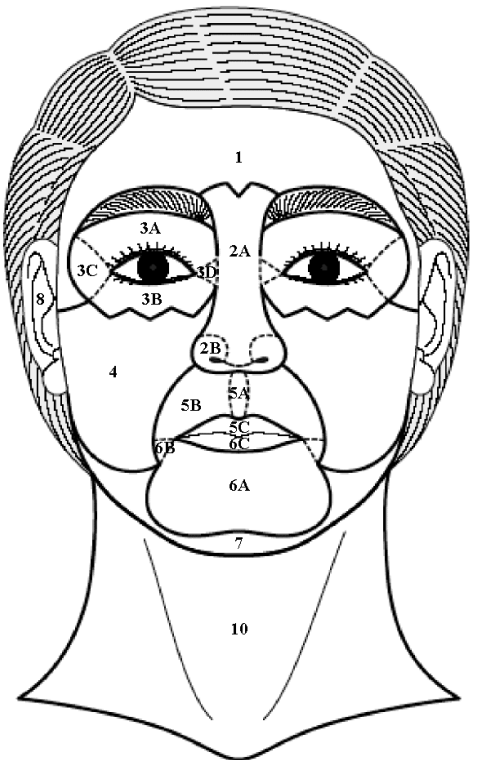
1. Forehead Unit

As described by Gonzarez-Ulloa 1), the forehead aesthetic unit is bound by the anterior hairline, the lateral temporal hairlines, an imaginary line connecting the lateral orbital rims to the lateral temporal hair line, and the supra-orbital brow and nasion. He also reported that the forehead skin is the thickest in the face: forehead: 2381 um, nasal lobule: 1764 um, cheek: 1509 um in patients ranging from 7 to 56 years old 1). Thus, deep burn reaching the frontal bone is relatively rare. If the bone is not exposed, a sheet of skin graft should be selected to aesthetically reconstruct the forehead. However, bone-exposed deep wounds require free flap transfer. Nevertheless, a large, single skin graft or flap should ideally be employed for forehead reconstruction. Connell 11) noted that transverse forehead creases and glabellar frown lines are important for normal appearance. Thus, when a sheet of skin graft cannot be applied at once, a joint line of grafts should be made transversally. We recommend the glabellar line in a triangular shape in order to prevent transverse contracture, as shown in Figure 1. This wedge is believed to prevent the glabellar frown.

Many methods have been reported related to eyebrow reconstruction, including the superficial temporal artery island flap 12,13), the prefabricated hairy flap 14), the composite graft from the scalp 15,16), and hair transplantation17,18). As Motamed 12) mentioned, the absence of eyebrows or distortions in their position alter the character of the face. Thus, eyebrow repair or reconstruction can be an important "finishing touch" in the overall reconstruction of a burned face 12). We should select these reconstructive methods on a case by case basis, and eyebrow reconstruction should be considered independent of forehead reconstruction.

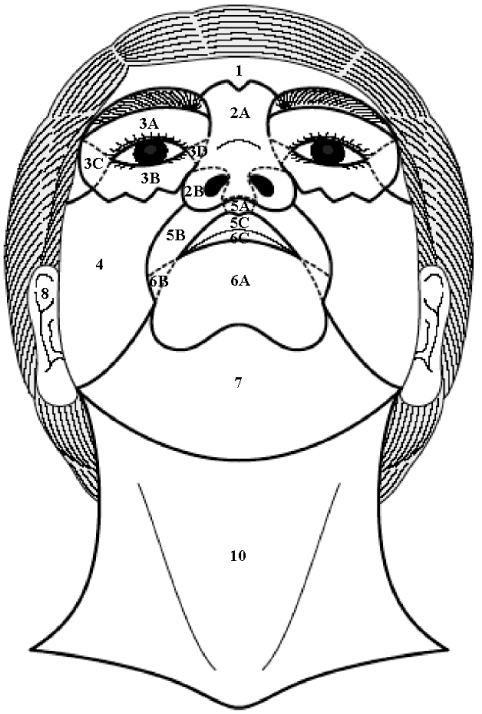


a. Frontal view.



b. Maxillary view.

Figure 1. (Continued)



c. Profile view.

Figure 1. The schema of "Reconstructive Units". 1: Forehead unit, 2: nasal unit (2A: dorsal nasal subunit, 2B: nasal alar subunit), 3: eyelid unit (3A: upper eyelid subunit, 3B: lower eyelid subunit, 3C: lateral canthal subunit, 3D: medial canthal subunit), 4: cheek unit, 5: upper lip unit (5A: philtrum subunit, 5B: lateral upper lip subunit, 5C: mucosal upper lip subunit), 6: lower lip unit (6A: central lower lip subunit, 6B: oral angular subunit, 6C: mucosal lower lip subunit), 7: mental unit, 8: auricular unit, 9: nape unit, 10: anterior neck unit.

2. Nasal Unit

Manson et al. 19) described a simplified technique incorporating the soft tissue cover, lining, and framework. Use of the aesthetic unit and subunit in the soft tissue cover seems appropriate. Burget et al. 6) reported that the complete subunit (if convex subunits are involved) must be replaced when major damage (>50%) is present. However, healthy skin should not be excised. As Rohlich et al. 20) described, aesthetic subunits essentially move irregularities from the center of a subunit to the borders between subunits. Similarly, we believe alar subunits reconstruct three dimensional configurations well, but other subunits such as dorsal side wall subunits are not essential for extensively burned patients. The nasal unit is composed of a dorsal subunit and an alar subunit in our "burn reconstructive units" (Figure 1). Medial canthus subunits of eyelids exist next to the dorsal nasal subunit. Use of the medial canthus subunits for dorsal nasal reconstruction prevents contracture of the medial canthus region.

The forehead flap 21, 22) or prefabricated flap 23, 24) can be employed for deep burns requiring lining and framework reconstruction or total reconstruction. In these cases, a sheet

of flap should be used, but nasal subunits are not essential for these total or subtotal nasal reconstructions.

3. Eyelid Unit

Eyelid burns occur in about 10% of thermal injuries and pose a considerable challenge for the reconstructive surgeon 25). Complete eyelid loss from burn is rare but sometimes occurs 26). If the orbicularis oculi muscle is damaged, local flaps 27, 28) or free flaps 26) must be selected on a case by case basis if possible. In these cases, flap shape should be applied to aesthetic units. However, non-damaged components including muscle and tarsal plates must be preserved.

If the muscle is minimally damaged, the reconstructive method should be limited to the skin graft. Split thickness grafts for the mobile upper eyelids and full thickness skin grafts for the lower lids have been routinely used 25). Full thickness skin grafts are ideal for preventing contraction, but have been considered unsuitable for use in the upper eyelid due to lack of suppleness 25). However, Lille et al. 29) reported that the treatment of acute eyelid burns with full-thickness rather than split-thickness skin grafts results in less ectropion and fewer reconstructive procedures.

Our "burn reconstructive unit" is shown on the lower eyelid (Figure 1). Skin graft edges should be in a zig-zag shape, as shown in Figure 1, to prevent gross contracture on the lower eyelid. On the other hand, the lateral and medial canthus subunits should form a triangular shape, and can be used for both upper and lower eyelid reconstruction, on a case by case basis. In addition, the medial canthus subunits effectively prevent scar contracture of the medial canthus region when either the upper eyelid or dosal nasal region is grafted. Additionally, Murakami et al. 30) reported that external wire frame fixation for temporary assistance of eyelid graft overcomes the disadvantage of tarsorrhaphy. These techniques may be useful for total care of eyelid grafts.

4. Cheek Unit

In the primary cheek reconstruction, a sheet of skin graft (full-thickness or thick split-thickness) or thin flap should be applied if a large part of the cheek was burned. In this respect, our "burn reconstructive units" do not have cheek subunits. If healthy skin exists around the cheek, the cervicofacial flap 31) and Juri flap 32) should be considered. Color and texture match of facial skin (and areas above the clavicle) is much more important than for other sites. Thus, we should try not to sacrifice healthy skin for aesthetic units or subunits more than is necessary, i.e., only for tangential excision. However, prevention of lower eyelid ectropion at the same time is important. Juri et al. 32) recommended use of anchor sutures to the periosteum along the zygomatic arch and inferolateral orbital rim. Moreover, the zig-zag line (Figure 1) will help release contracture of the lower eyelid.

The aesthetic results of thin flaps are sometimes better than skin grafts in secondary reconstructions, or skin resurfacing 33-35). However, expanded skin flaps, and sometimes expanded distant flaps, should provide ample large flaps from the site close to the face. Thus, these two or three stage operations are disadvantageous. Therefore, we have selected the full-

thickness skin graft as a one stage operation or the expanded skin flaps as a two or three stage operation on a case by case basis. Free flaps, including perforator flaps, have been used for facial reconstruction 36, 37), but the color and texture match is poor. Thus, free flaps from distant sites should not be used for skin resurfacing of the cheek.

5. Upper Lip Unit

Examination for respiratory tract burn is a necessary part of acute peri-oral burn treatment, while treatment to prevent contracture should be started simultaneously. The vascular pedicled flap such as the submental artery flap 38) or submental perforator flap 39, 40) are useful for reconstruction of deep burns in which the orbicularis oculi muscle is damaged. These flaps are harvested from the beard region, and therefore simultaneous reconstruction of the upper lip and mustache can be planned in male patients. On the other hand, Chang et al. 41) reported the long term results of total upper lip reconstruction using the temporal flap, with a single-staged, relatively simple method of providing hair-bearing skin to the upper lip. Moreover, Hyakusoku et al. 42) described a prefabricated flap using a vascular bundle transfer. Of course, the free flap is another good option. Langstein et al. 43) mentioned that free tissue transfers, such as the free radial forearm flap, are useful for larger defects, as they import additional tissue in one step and reduce the incidence of microstomia, which is more likely to result from local tissue repairs.

Skin grafting is a good indication if the orbicularis oculi muscle is not damaged, and the grafts and flaps should be employed to apply "burn reconstructive units." Reconstruction of the medial upper lip unit is important for favorable aesthetic results, and the philtral dimple should be reconstructed primarily or at least secondarily. Secondary reconstructions performed with composite grafts such as ear skin and cartilage are generally successful 44). The most important feature of the "burn reconstructive unit" on the upper lip is the lateral upper lip subunit, which was designed for use as an oral angular subunit on a case by case basis in order to prevent commissure contracture. Ample debridement and sufficient tissue augmentation effectively prevent contracture.

6. Lower Lip Unit

Except in cases of deep burn exposing the mandible bone, skin grafts should be large enough to prevent ectropion of the lower lip. As Neale et al. 45) mentioned, important considerations of peri-oral burn treatment are the choice of unit release or simple release, the choice of donor site to match the remaining facial skin, and the timing of the reconstruction 45). The oral angular subunit (Figure 1**)** should be used with the central lower lip unit for a consecutive wound to the commissure and/or the upper lip. A consecutive wound to the anterior neck should be reconstructed with a large thin sheet flap to cover both the lower lip and the anterior neck. The submental artery flap 38) or submental perforator flap 39, 40) are useful for simultaneous reconstruction of the lower lip and beard region in male patients. Dermiz et al. 40) reported a lower lip scar and distortion case reconstructed with the submental artery perforator flap, which released contracture and reconstructed the beard region to achieve both functionally and aesthetically positive results.

7. Mental Unit

The most common problem for post burn patients is hypertrophic scar formation 46). Subdermabrasion and full-thickness skin grafting are treatment options for hypertrophic scar, as Silfan et al. 46) reported. If burn wounds exist on both the mental region and the lower lip, the central lower lip subunit and the mental unit can be considered as one. Contracture between the lower lip and the anterior chest cause a severe facial deformity, so skin graft should be used to release or prevent contracture. A sheet of thin flap can be used to reconstruct consecutive scar contractures on both the mental region and the anterior neck. The mentocervical angle and submental crease can be reconstructed by a sheet of thin flap. Thus, the medial lower lip unit, the mental unit, and the anterior neck unit do not always need to be separated for extensively burned patients, especially for cases that are reconstructed using a thin flap sheet.

8. Auricular Unit

Ear reconstruction is performed in extensively burned patients primarily for functional reconstruction of the auriculotemporal sulcus, so that a mask or glasses may be worn. Auricular aesthetic subunits are influenced largely by cartilage lining, so prevention of auricle cartilage deformity is important. In other words, skin grafts over the subunits do not impact aesthetic results if the cartilage shape remains stable. Thus, direct thermal injury of auricle skin 47) and subsequent chondritis 48) should be treated early. Direct closure 49) or use of a chondrocutaneous advancement flap 50) are useful for small wounds. Postauricular skin, such as Dieffenbach's flap 51), can be used to reconstruct much larger defects. The shape of the cartilage framework is of paramount importance for total ear reconstruction, so aesthetic subunits are not essential when the framework is covered by temporoparietal fascia and skin graft 52).

9. Nape Unit

The posterior neck and postauricular area generally do not require either aesthetic or functional reconstruction; even severe scars can be covered with hair. However, hypertrophic scars or keloidal formation can occur with folliculitis in this area 53). In such cases, the causative bacteria and fungus must be treated, and skin grafting may be indicated.

10. Anterior Neck Unit

The anterior neck is a region with multidirectional and complex motility. Moreover, the region is connected to the lower face. Thus, scars on the neck directly influence facial movement. Patients affected in this region usually have severely restricted neck motility, stiffness in the shoulders, headaches, and lower lip ectropion 54). Many operative procedures have been reported including z-plasty 53), local flap 55), skin graft 55, 56), expanded flap 33, 34, 57), regional flap 58), free flap 59, 60), perforator flap 61), and thin flap 62-67). Z-plasty

is useful for small band contracture, but not for planer contracture. The greatest problems associated with skin grafting (even full thickness) are poor aesthetic results and re-contracture. Expanded flaps are sometimes useful, since thin and large flaps can be employed from the anterior chest or the back for aesthetic improvement. However, this procedure must be performed as two or three stage reconstruction. Large, thin flaps must be used for complete functional and aesthetic reconstruction 54), and perforator flaps are limited in size. In summary, the anterior neck should be reconstructed with an extremely thin and large flap. Contracture can be completely released by reconstruction with a sheet of flap between the submental crease and the upper edge of the clavicle in one stage.

More than fifteen years of experience have made us confident that the "super-thin flap" harvested from the dorsal region is the best option for reconstructing areas around the anterior neck 62-67). A discriminating feature of the flap is its extremely thin form. It is primarily thinned to the layer where the subdermal vascular network (subdermal plexus) can be seen through the minimal fat layer. In many cases, these flaps can be harvested as skin pedicled flaps. Moreover, much longer and larger flaps can be harvested according to the selection of the perforators attached to the flaps, making these flaps "made-to-order flaps." As Angrigiani et al. 68) reported, ample skin flaps can be harvested to reconstruct the anterior neck for full facial reconstruction with dorsal skin.

CONCLUSION

We revisited the concept of "aesthetic units" and "aesthetic subunits" by reviewing the literature. Our "burn reconstructive units" were categorized into 10 units: 1. forehead unit, 2. nasal unit, 3. eyelid unit, 4. cheek unit, 5. upper lip unit, 6. lower lip unit, 7. mental unit, 8. auricular unit, 9. nape unit, and 10. anterior neck unit. "Burn reconstructive units" were designed to prevent and release scar contracture in addition to improve aesthetic outcomes. Thus, the concept of "burn reconstructive units" can be considered as "functional units" in contrast to "aesthetic units." Burn reconstructive surgeons must perform reconstructions for both functional and aesthetic outcomes, and should consider many options to deal with various problems caused by burns on a case by case basis.

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Chapter 8

USE OF MODERN DAY TECHNOLOGY FOR PAIN MANAGEMENT DURING BURN INJURY REHABILITATION

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INTRODUCTION

With advances in medicine bringing about significant improvements in critical burn care management; the chances of surviving even the most extensive burn injury are high (Connor-Ballard et al 2009). Needless to say, individuals who sustain extensive burn injuries and indeed survive are often left with severe physical disabilities and require comprehensive burn care management and rehabilitation for longer periods of time (Lončar et al 2006; Patterson et al 2007). Burn rehabilitation is primarily aimed at reducing the development of physical complications and minimizing functional disability; ensuring prompt societal re-integration and optimal quality of life post-injury (Pruitt et al 2009; Sen et al 2009). Rehabilitation therefore remains, and will probably always be, an indispensable component of burn care management programs (Richardson et al 2009; Sen et al 2009).

Rehabilitation in itself, however, is an arduous process since the specific techniques utilized by therapists, mechanically elicit tremendous amounts of pain which may increase anxiety levels in patients and lead to non-compliance towards further rehabilitation. Since non-compliance compromises successful implementation and progression of rehabilitation; adequate management of pain and pain-related anxiety during the rehabilitation of a burn injury patient is crucial in ensuring the achievement of optimal functional outcomes (van Baar et al 2006; Haik et al 2006; Summer et al 2007; van Twillert et al 2007; de Jong et al 2007).

The following chapter presents the current challenges experienced in the management of pain during burn injury rehabilitation and the use of modern day technologies as part of a multi-modal pain management approach in burn care, with special focus placed on the current evidence into the efficacy of Virtual Reality (VR) on pain and anxiety experienced in burn injury patients during rehabilitation.

THE RECOVERY PROCESS FOLLOWING A BURN INJURY

The recovery process for a burn injury commences as soon as the victim is admitted to the emergency unit at the hospital, and continues for approximately one year after discharge. The recovery process consists of 3 phases based on various pathological responses which occur locally and systemically after sustaining a burn injury, and are commonly referred to as the *acute-; healing-;* and *remodelling/rehabilitation* phases. The phases of the recovery process for a burn injury are described as follows (Wiechman et al 2004; Summer et al 2007):

- The *acute phase* is the period following a burn injury during which excessive fluid replacement is required to maintain circulating volume. Once the patient is stabilized, initial wound debridement is performed. Depending on the severity of the burn injury, the acute phase may last for two to three days or be completely bypassed;
- The *healing phase* is the period during which healing of the burn wound is aided. Successful healing requires a clean wound bed, which is typically accomplished through frequent dressing changes and debridement of the wound. The healing phase typically lasts for a few weeks;
- The *remodelling* or *rehabilitation phase* is the final phase of the recovery process for a burn injury and is the period during which the inflammatory response and remodelling of tissue subsides, resulting in the scar tissue at the burn site becoming softer, less reddened and flatter. The remodelling phase usually lasts for up to one year, but may last for much longer depending on various factors i.e. age of patient; extent of burn injury; development of complications; etc.

COMMON COMPLICATIONS ARISING FROM A BURN INJURY

Long periods of immobility following a severe burn injury are typical as patients are often admitted to the intensive care unit (ICU) in a critical condition. Without intervention and attempts to mobilize the patient as soon as possible, the neuromusculoskeletal and respiratory systems can be compromised. Within 2-3 weeks, the skin will lose its elasticity and contract; tendons and muscles will shorten; muscles will weaken; joint range of motion (ROM) will decrease and circulatory problems will occur, risking the development of various complications.

The most common complications which may develop as result of immobilization following a burn injury include (Esselman et al 2007):

- muscle atrophy
- contractures
- hypertrophic scarring
- heterotrophic ossification
- vascular/circulatory complications
- neurological pathology
- respiratory complications

In most instances, the development of physical complications i.e. contractures may be an indication for surgical intervention, which in itself is associated with additional complications. The development of respiratory complications i.e. atelectasis or pneumonia on the other hand, may influence overall fitness and endurance levels, limiting participation in rehabilitation. Similarly, the development of vascular complications i.e. gangrene may result in amputation of a limb, which may further hamper rehabilitation and the achievement of optimal functional outcomes.

The development of complications following a burn injury therefore significantly influences rehabilitation and compromises the achievement of optimal functional outcomes and quality of life post-injury. Early detection and appropriate management, as well as the early introduction of comprehensive rehabilitation are essential in preventing the development of burn-related complications and minimizing functional disability.

REHABILITATION OF A BURN INJURY

Comprehensive rehabilitation programs are usually introduced during the early stages of the burn injury recovery process and are modified accordingly to accommodate the patient's needs as recovery progresses. For the majority of individuals who have sustained an extensive burn injury, rehabilitation continues for many years after re-integration into society.

The following section discusses the specific aims, goals and content of rehabilitation programs at various phases of the burn injury recovery process.

Primary Aims and Goals in Burn Rehabilitation

The primary aim of rehabilitation following a burn injury is to maintain the integrity of the neuromusculoskeletal system by maintaining muscle bulk and strength; joint ROM; muscle and tendon length; skin elasticity and vascular tone; essentially preventing or minimizing the development of physical complications and functional disability; and achieving the following rehabilitation goals:

- regain or maintain maximum independence
- prompt return to pre-injury functional status (or as close as possible)
- prompt re-integration into society
- prompt return to family role/obligations
- prompt return-to-work
- optimal post-injury quality of life

Role of Rehabilitation during the Recovery Process of a Burn Injury

Each phase of the burn injury recovery process provides an ideal opportunity for the various goals of rehabilitation to be accomplished. In figure 1, the main focus of rehabilitation at various phases of the recovery process following a burn injury is depicted (Civaia et al 2003):

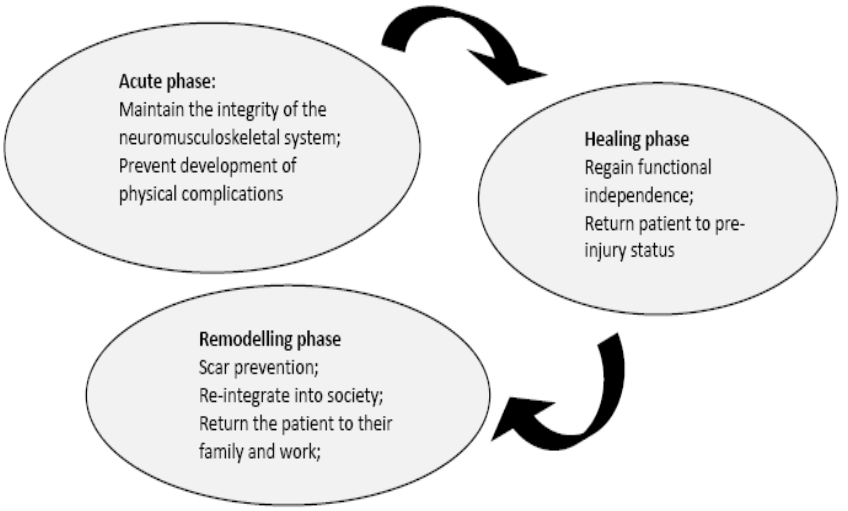

Figure 1. Rehabilitation goals during the recovery process of a burn injury (Civaia et al 2003).

Burn Care Management and Rehabilitation Team

A holistic multidisciplinary approach in burn care management and rehabilitation is essential since the various specialties of each discipline within the multidisciplinary team are brought together to ensure optimal achievement of patient clinical and functional outcomes (Falder et al 2009). The availability and involvement of the health professionals in the multidisciplinary management of a burn injury patient is however often limited to larger burn institutions and the need for each discipline diminishes as recovery progresses and the patient's requirements change. The medical and allied health disciplines typically involved in the management and rehabilitation of burn injury patients include:

- Anaesthetists / Pain management specialists
- Dieticians / Nutritionists
- Medical/Surgical specialists
- Nursing practitioners
- Occupational therapists
- Orthotists / Prosthetists
- Physiotherapists
- Psychiatrists / Psychologists
- Social workers
- Speech therapists

Burn Rehabilitation Programs

Successful rehabilitation in burn care is dependent on the skills and commitment of the rehabilitation therapists and medical staff; the quality and accessibility of health resources;

the design and content of the rehabilitation program; the family and social support structure; as well as the patient's compliance towards rehabilitation and the level of trust placed in the therapist (van Twillert et al 2007; de Jong et al 2007). Physiotherapists and Occupational therapists are specifically involved in the design and delivery of rehabilitation programs in burn care management. The therapists utilize various techniques and modalities throughout rehabilitation; choosing the most appropriate management strategy to ensure rehabilitation goals are met at each phase of the recovery process of a burn injury. Rehabilitation programs are designed to accommodate the requirements of the individual patient and are modified accordingly as recovery progresses.

Mobilization techniques and rehabilitation exercises form a large part of burn injury rehabilitation programs and are primarily used to maintain muscle and tendon length, skin elasticity, muscle strength and joint ROM; ultimately preventing the development of physical complications and minimizing functional disability.

Common mobilization techniques/rehabilitation exercises used by therapists during burn injury rehabilitation include (Civaia et al 2003; Esselman et al 2007):

- passive mobilization exercises
- stretching techniques
- joint ROM exercises
- specific assisted-active mobilization
- active mobilization exercises
- mobilization against resistance/strengthening exercises
- static-dynamic exercises
- proprioceptive re-education
- re-education of functional activities

In addition to the mobilization techniques and exercises mentioned, the following modalities and techniques are often incorporated to further assist in optimizing rehabilitation, and are specifically targeted at preventing contractures and hypertrophic scarring, and maintaining joint ROM (Civaia et al 2003; Esselman et al 2007):

- Massage (scar massage) therapy: improves circulation within scar; reduces oedema and itching; increases the elasticity of the skin; desensitizes skin; breaks down adhesions; strengthens the skin and improves appearance of skin
- Manual lymphatic drainage: repairs venous and lymphatic circulation and drainage; reduces oedema; prevents the development of fibrous tissue and adhesions
- Ultrasound: reduces oedema; prevents the attachment of adhesions and fibrous tissue
- Vacuum therapy: breaks down adhesions by increasing and decreasing pressure within scar
- Pressure garments: provides continuous pressure to the healing skin
- Splinting: aids in maintaining joint ROM

The various mobilization techniques or rehabilitation exercises incorporated in a typical burn injury rehabilitation program, are either performed with the help of the therapist; against resistance provided by the therapist; autonomously by the patient; using complete kinetic

chain movements; or using single isolated movements (Civaia et al 2003; Esselman et al 2007).

CHALLENGES IN BURN INJURY REHABILITATION

The intentional manoeuvring of the healing burn wound sites during rehabilitation, mechanically elicits a significant amount of pain, causing increased levels of anxiety. Consequently, trust between the therapist and patient is broken hindering patient compliance towards rehabilitation and compromising functional outcomes. Adequate management of pain during the rehabilitation of a burn injury patient is therefore necessary to avert the cycle of pain and anxiety; maintain a trusting patient-therapist relationship; ensure patient compliance and achieve optimal functional outcomes, independence and quality of life post-injury (Haik et al 2006; van Twillert et al 2007; de Jong et al 2007).

The following section discusses the challenges faced in adequately managing burn injury pain and the specific influence pain and subsequent anxiety experienced during burn injury rehabilitation has on achieving successful functional outcomes.

Burn Injury Pain

Burn injury pain is arguably one of the most excruciating types of pain known to mankind and the most difficult type of acute pain to manage (Lončar et al 2006). The challenges faced in adequately managing burn injury pain can mainly be attributed to the unique and multi-dimensional qualities of burn injury pain as well as related factors such as anxiety.

According to the IASP, three classifications of burn injury pain exist; namely *background* -, *breakthrough*- and *procedural* pain (IASP 2001). The three types of burn injury pain are experienced at different phases of the recovery process and are elicited through various activities or procedures. The characteristics of the various types of burn injury pain are depicted in Table 1.

Relationship between Pain and Anxiety in Burn Rehabilitation

For many years, the relationship between pain and anxiety has been investigated. Theories derived from these studies seem to be focused on the fact that pain and anxiety are positively correlated (Ploghaus et al 2001, Abdi et al 2002). Pain-related anxiety before and during a painful procedure, will in turn exacerbate the pain levels during the procedure, leading to further anxiety and more pain. Therefore, if burn injury pain is not adequately controlled during rehabilitation, anxiety becomes a part of the entire burn injury process, hindering patient compliance and compromising overall rehabilitation outcomes (Lončar et al 2006). In figure 2, the "pain and anxiety" cycle which typically results from the inadequate management of pain in burn care is depicted.

Table 1. Comparison of characteristics of various types of burn injury pain (IASP 2001)

Type of pain Characteristics	Background	Breakthrough	Procedural
Eliciting mechanism/activity	rest /during periods of immobility	normal movements / daily activities / bed activities	procedures such as wound dressing changes / mobilization techniques
Description of sensation	'continuous', 'burning' or 'throbbing' sensation	'stinging', 'pricking', 'shooting' and 'pounding' sensation	'excruciating', 'intense' 'burning' and 'stinging' sensation
Duration	Usually prolonged	Usually temporary and comes on suddenly	Usually continues throughout procedure, but continue for a few seconds or longer after procedure has ended
Intensity	Mild to moderate	Moderate	High

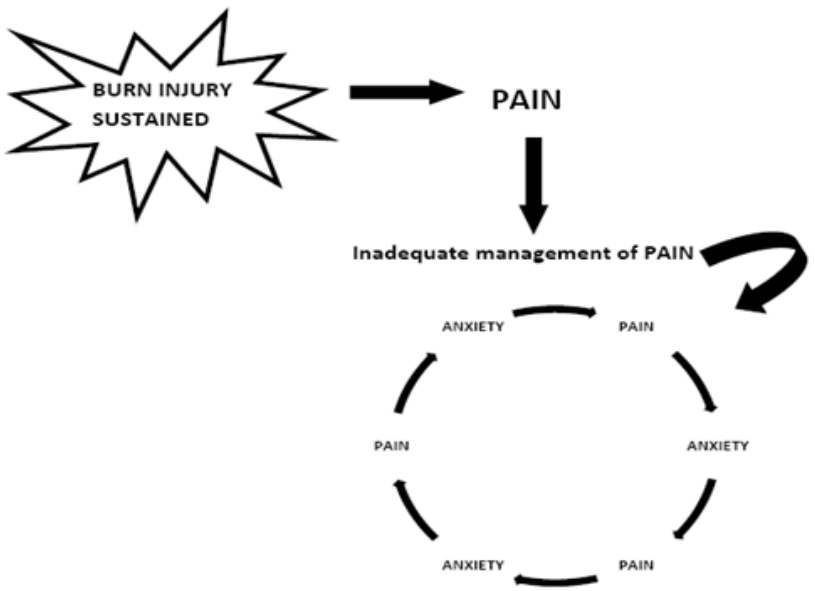

Figure 2. Pain and anxiety cycle in burn injuries (Lončar et al 2006).

Challenges in the Pharmacological Management of Procedural Pain during Rehabilitation

Traditionally, therapists have relied on the exclusive use of pharmacologic analgesics i.e. short-acting, potent opioids, to modulate the burn injury patient's pain and related anxiety

during rehabilitation. However, due to the adverse effects and inherent limitations linked to the excessive use of opioids; the safety of the patient is frequently prioritized above the need for adequate pain management; resulting in the under-treatment of burn injury pain (Summer et al 2007; Richardson et al 2009). Pain experienced during burn injury rehabilitation therefore remains inadequately managed and continues to challenge health professionals globally (van Baar et al 2006; Haik et al 2006; van Twillert et al 2007). Since uncontrolled procedural pain during rehabilitation is significantly detrimental and contributes to patient discomfort, dissatisfaction, despondency and distress, and directly affects rehabilitation outcomes; the exclusive use of pharmacologic analgesics during burn injury rehabilitation was reviewed and modified accordingly.

Multi-modal Analgesia Management Approach

In 2001, the International Association for the Study of Pain (IASP) suggested that to adequately reduce pain and related anxiety; minimize adverse drug effects; increase patient compliance and maximize functional outcomes, a "multi-modal analgesia management approach" in burn care had to be implemented and should typically include the use of appropriate pharmacologic analgesia, as well as incorporate non-pharmacological, non-invasive analgesia adjuncts which are associated with minimum side-effects (IASP 2001; Summer et al 2007).

A number of non-pharmacologic, non-invasive adjuncts to pharmacologic analgesics have been used in the management of pain and pain-related anxiety experienced during burn care management and rehabilitation and includes the following:

- Music therapy
- Imagery
- Distraction i.e. VR
- Video game technologies
- Attention-focusing techniques
- Hypnotherapeutic techniques/Hypnosis
- Cognitive Behavioural techniques (CBT)
- Relaxation therapy
- Progressive muscle relaxation
- Deep breathing exercises
- White noise therapy
- Aromatherapy
- Transcutaneous electrical nerve stimulation (TENS)
- Patient education and preparation

Keeping within the scope of this chapter, modern day technologies i.e. VR will be discussed in the section which follows.

VIRTUAL REALITY: A MODERN DAY TECHNOLOGY FOR BURN INJURYPAIN DURING REHABILITATION

Coinciding with the rapid implementation of technology in virtually all aspects of life today; the use of modern day technologies as non-pharmacological, non-invasive adjuncts to traditional pharmacologic analgesics has received considerable attention. One specific modern day technology has literally taken the medical field by storm and is currently the main focus in pain management and rehabilitation research.

The following section presents the current evidence into the effect of VR as a non-pharmacologic and non-invasive adjunct to traditional pharmacologic analgesics in the management of pain and anxiety during burn injury rehabilitation.

Current Definition of VR

VR is an advanced form of human-computer interface which allows a user to immerse and interact with a 3D computer-generated environment (or virtual world). The virtual environment is simulated from a real or imaginary scenario. The experience of immersion is engrossing and gives the perception of actually being in the virtual environment. VR environments are primarily visual experiences, displayed either on a computer screen or through specialized stereoscopic displays. Visual, auditory and touch sensations can be added or modified based on the stimuli and purpose of the VR application, enhancing the virtual experience and increasing the immersive properties (Schultheis et al 2002; Das et al 2005).

VR Equipment

VR systems typically consists of head-mount displays (HMD), tracking systems, earphones, speakers, and haptic-feedback devices. The HMD is an image display system worn on the head. A tracking system which is usually inserted in the HMD, senses position and orientation of the user and relays that information to the computer screen in real-time, causing the avatar (a computer-generated representative) in the virtual environment to mimic the user's movements. Users can interact with the virtual environment via haptic-feedback devices such as a mouse, joystick or keyboard, or specialized equipment like interactive or motion-sensing gloves or body suits. Some VR systems incorporate the use of 3D projection walls or rooms instead of HMDs. Regardless of the types of display used, maximizing immersion and interactivity in the virtual world is the main priority of VR to ensure that a complete "sense of presence" and "believability" in the virtual world is achieved (Schultheis et al 2002).

VR Applications

During the 20^{th} and particularly the 21^{st} century, advances in technology allowed for the concept of VR to be taken to another level. With the simulation of various real or imaginary virtual environments for any scenario, the use of VR is currently applied in the medical and medically-related fields (i.e. psychology and allied health), as well as non-medical fields (i.e. in the military, industry and the media).

In the medical and medically-related fields, the use of VR is based on diagnosis and management. The mechanisms through which VR work depend on the condition and the goals of management. For instance in pain management, VR is used as a distraction technique

(i.e. pain management); in the treatment of phobias i.e. arachnophobia, VR is used as an exposure therapy; and in the rehabilitation of neuromusculoskeletal disorders, VR is used as a task-orientated rehabilitation tool.

Applications in medical and medically-related fields include the following:

- Treatment of post-traumatic stress disorder (PTSD)
- Treatment of anxiety disorders and phobias i.e. arachnophobia, fear of flying, fear of heights
- Pain management i.e. during burn wound care procedures and rehabilitation
- Rehabilitation of stroke and other neurological conditions
- Rehabilitation of orthopaedic conditions
- Sport rehabilitation
- Treatment of Attention Deficit and Hyperactivity disorders (ADD and ADHD)
- Treatment of various eating disorders
- Medical training
- Dentistry
- Injections

Non-medical applications of VR include the following:

- Entertainment and gaming
- Military/ Defence training
- Road safety education
- Advertising/marketing
- Corporate applications
- Industrial applications
- Architectural designing/Town planning

Mechanism of VR as a Distraction Technique

The application of VR as a distraction technique is based on the assumption that pain perception has a large psychological component and attracts a strong attentive response because of the potential threat of damaged tissue associated with the sensation. By re-directing the attention or distracting the patient away from the pain stimulus, pain perception is manipulated and the intensity of the pain is reduced (Wismeijer et al 2005; Dunckley et al 2007). VR provides significant cognitive distraction as it is immersive and interactive, and has the ability to block visual and aural input from the hospital surroundings. The more immersive the VR system, the more the patient's attention will be drawn into the virtual world, leaving less attention available to process pain experienced during a painful procedure. Furthermore, since the patient may also become less anxious towards the procedure, the cycle of pain and pain-related anxiety may essentially be averted, further reducing pain (figure 2) (Lončar et al 2006). A recent functional magnetic resonance imaging (MRI) study also found that VR actually reduces the amount of pain-related brain activity and changes the way incoming pain signals are interpreted (Hoffman et al 2007), providing empirical evidence into the neurophysiological mechanism of VR in reducing pain. Further research is however warranted to reiterate these findings.

Evidence for the Use of VR in Pain Management during Burn Injury Rehabilitation

The origins for the use of VR in the modulation of procedural pain and anxiety during burn injury rehabilitation arose from the recognized need for improvement in traditional burn pain management regimens and the inadequacy and limitations related to the exclusive use of traditional pharmacologic analgesia such as opioids (Hoffman et al 2000; de Jong et al 2007). As a non-invasive and non-addictive distractive analgesic technique, VR has minimal side-effects associated with it, making it a safe adjunct to pharmacologic analgesics and other harmful agents typically administered in the management of burn injury pain (Morris et al 2009; Hoffman et al 2011). The evidence that VR cognitively distracts the patient's attention from the painful procedure and reduces neurophysiological activity in pain centres thereby altering pain perception and reducing anxiety levels; offers a valuable rationale for the implementation of VR as part of a multi-modal analgesia approach to adequately manage pain and related anxiety and to ensure optimal functional outcomes are achieved in burn injury rehabilitation (IASP 2001; Sharar et al 2008; Morris et al 2009; Hoffman et al 2011).

For more than a decade, the advantages of VR have been widely studied and recognized within the clinical burn setting, supporting for the use of VR as a safe and effective non-pharmacologic and non-invasive adjunct to traditional pharmacological analgesia in burn pain management (Morris et al 2009; Hoffman et al 2011). Until recently, the evidence into the efficacy of VR on pain and related anxiety in burn care management was however largely provided by small, non-randomized trials (Morris et al 2009). In 2011, a randomized controlled trial into the effect of VR on pain, anxiety and ROM experienced by 54 burn patients aged 16 to 19 years old during physical therapy was conducted (Schmitt et al 2011). The results of the trial indicated that VR significantly decreased pain ratings by 27% to 44% and that the analgesia effect and treatment improvements were maintained with repeated use over multiple therapy sessions. Although larger, randomized controlled trials are further warranted, the current study provides high level evidence for the effect of VR as an adjunct in pain management during burn care which has not previously been available.

Patient comfort and compliance during wound care and rehabilitation, as well as successful healing of the wound, is essential in achieving optimal functional outcomes and quality of life post-injury. The challenges previously faced due to the inadequate management of burn injury pain during wound care and rehabilitation can now be addressed without additional risk factors and side-effects involved. While pharmacological analgesia cannot completely be eliminated from the burn pain management regime for ethical reasons as yet, the increasing evidence for VR currently provides health professionals with a safe, exciting and technologically-advanced supplementary tool to make the rehabilitation process, as well as the entire recovery process for burn injury patients less excruciating, less distressful and improve patient compliance to ensure optimal functional outcomes (Morris et al 2009; Hoffman et al 2011).

The Use of Low-cost VR Video Game Technology in Pain Management during Burn Rehabilitation

In 2006, the use of the Sony Playstation II EyeToy (Sony Corporation, Foster City, CA, USA) in the rehabilitation of burn patients was investigated. The study reported that the Sony Playstation II EyeToy seemed to reduce pain and anxiety, as well as heighten the level of patient co-operation, which is essential for the successful rehabilitation of burn patients (Haik et al 2006). Although a single-subject case study, the preliminary results of this study justified

the use of a simple, commercially-available and low-cost VR system. Further research is however warranted.

Recently, the use of a more advanced video game technology, namely the Nintendo® Wii™ and WiiFit (Nintendo of America Inc., Redmond, WA, USA) in rehabilitation also referred to as "Wiihabilitation" has been reported (Anderson et al 2010; Fung et al 2010; Levac et al 2010; Foley et al 2010). The aims of these studies were mainly to enhance rehabilitation programs currently delivered by physiotherapists and occupational therapists. The results of the studies showed that the implementation of the Nintendo® Wii™ was successful in increasing patient motivation and encouraging full body movement. The Virtual Wiihab, developed by Anderson et al in 2010, currently does what no other low-cost VR systems do. It is able to record performance and behavioural measurements; allow for activity customization and use auditory, visual and haptic elements to provide extrinsic feedback (Anderson et al 2010). Further research is however warranted.

In 2011, the efficacy of the Nintendo® Wii™ on pain, anxiety, active ROM and function experienced during burn rehabilitation was investigated (Yohannan et al 2011). The study included 23 adult subjects aged 20 to 78 years. The study reported that the difference in mean slopes suggested that the Wii group experienced less pain than the control group over time. In addition, the overall trends observed in anxiety, active ROM and function seemed to improve at a faster rate in the Wii group (Yohannan et al 2011). Although larger, randomized controlled trials are required; this study provides preliminary evidence for the use of the Nintendo® Wii™ in the management of pain during burn rehabilitation.

Low-cost VR Systems for Developing Countries

Although the first case study investigating the effect of VR in conjunction with pharmacologic analgesics, on burn injury pain was published almost 12 years ago (Hoffman et al 2000), research into the effect of VR on pain and anxiety experienced by burn patients during wound care procedures and rehabilitation has literally only exploded over the past three years.

In 2009, a systematic review reported that only nine small studies into the effect of VR on burn injury pain during wound dressing changes and rehabilitation had been conducted, of which none were conducted in developing countries (Morris et al 2009). At the end of 2011, more than 40 studies into the use of VR in burn injury pain had been published, illustrating the growing interest in the topic. It however remains disconcerting that the majority of the recent studies are still conducted in developed countries, reducing the generalizability of the results to poorer nations. Furthermore, the VR systems utilized in these studies are generally expensive and probably not economically feasible for use in lower-income nations where healthcare budgets are often constrained (Morris et al 2010). To date, only one pilot study (n=11) investigating the effect of a commercially-available, low-cost VR, the eMagin Z800 3DVisor (www.emagin.com) on procedural pain and anxiety during physiotherapy management in burn injury patients has been conducted in South Africa (Morris et al 2010). The study reported reductions in pain and anxiety by up to 50% in burn injury patients during physiotherapy management (Morris et al 2010). Although it can be argued that South Africa is technically no longer classified as a developing country; economically and in terms of availability of resources, South Africa remains at a disadvantage. More research into the effect of VR in the management of pain and pain-related anxiety experienced in burn care is

therefore needed in developing countries where burn injuries are more prevalent, more extensive and the burden of disease is often larger (Louw et al 2007).

Current Challenges in the Use of VR

Although the evidence into the effects of VR is increasing, the implementation of VR systems was and still is associated with a number of challenges such as lack of clinical acceptance; cumbersome wiring of equipment; heavy equipment; cost of equipment; lack of technical support; lack of staff and time; lack of computer training in therapists; inability to adequately resize or adjust equipment for paediatric patients; patient safety issues and limitations in sterilization of equipment. With advances in technology, the majority of these challenges have already or are in the process of being overcome and a few of these challenges have been addressed with the implementation of low-cost, commercially-available VR systems.

Compared to the expensive VR systems generally utilized in developed countries; the advantages of the commercially-available VR system used by Morris et al (2010) were as follows:

- Low-cost system
- Safe
- Required minimum technical experience
- Required minimum staff
- Required no additional allocation of time
- User-friendly
- Portable and lightweight
- Easy to store
- Re-usable
- Could be sterilized
- Local technical support was available

More research into the effect of this and other low-cost and commercially-available VR systems in the management of pain and pain-related anxiety experienced in burn care is however warranted.

CONCLUSION

Adequate pain control during burn injury rehabilitation is challenging, but is essential to achieve optimal functional outcomes and successful reintegration into society. The advantages of VR, a modern day technology, has become widely recognized within the clinical burn setting for its effect on reducing pain and associated anxiety experienced during burn injury rehabilitation and other medical procedures. Since the exclusive use of pharmacological analgesics has been found to be inadequate to manage procedural and rehabilitation pain, non-pharmacological and non-invasive modalities such as VR, which have minimum associated adverse effects, can be considered as safe adjunct therapies in burn pain management programs to assist health professionals and patients during burn injury

rehabilitation. Larger, well-designed randomized controlled trials, especially in developing countries, are however warranted.

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Chapter 9

CARBON MONOXIDE INTOXICATION IN BURNS

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1. ABSTRACT

Carbon monoxide (CO) intoxications are frequent and can lead to high morbidity and mortality, involving multiple organ systems (e.g. lung, heart, peripheral and central nervous system) and undetected CO exposure can be fatal. It is a toxic, colorless, odorless, tasteless, and non-irritating gas. From the available data, carbon monoxide poisoning is the most common cause of injury and death due to poisoning worldwide. Prevention remains a vital public health issue, requiring public education on the safe operation of appliances, heaters, fireplaces, and internal-combustion engines, as well as increased emphasis on the installation of carbon monoxide detectors. In Burns, CO intoxication CO binds hemoglobin 230-270 times more avidly than oxygen, so even small concentrations can result in significant levels of carboxyhemoglobin (COHb). The clinical picture is untypical and in many times is not related to the amount of COHb. In severe cases, CO intoxication can lead to coma or even death. In case of pregnancy, Carbon monoxide also crosses the placenta and combines with fetal hemoglobin, causing more direct fetal tissue hypoxia. Additionally, fetal hemoglobin (Hbf) has a 10 to 15% higher affinity for carbon monoxide than adult hemoglobin (HbA), causing more severe poisoning in the fetus than in the adult. Arterial blood gas (ABG) is one of the most reliable Investigations to detect the level of COHb but the main disadvantage of ABG with COHb testing is the unavailability in pre-hospital rescue conditions. To date, COHb is routinely used as a marker for detecting CO intoxication. It is suggested that the lactate level may be a useful prognostic factor, but this is still controversially discussed. As a basic role in the treatment, a An immediate supply of high dose oxygen is essential to reduce mortality and long-term morbidity. Furthermore, hHyperbaric oxygen therapy (HBO) is now standardized in many centers worldwide. Increased elimination of COHb clearly occurs but on the other hand, the benefit of HBO treatment is still under current

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debate. Treatment of CO intoxication could be very challenging especially those cases associated with Burns. Thus multidisciplinary approach should always be considered involving Burns surgeons, Emergency Room (ER) physicians, Otolaryngologists, Internists and Anesthesiologists.

2. BACKGROUND

Carbon monoxide (CO) is a colorless, odorless, tasteless, and non-irritating gas. It is a product of incomplete combustion of organic matter with insufficient oxygen supply. Thus, it must be suspected in every burn case. The pathophysiology of CO intoxication is not fully understood but a lot of studies and researches were focused on this point in the last decades describing the mechanism. As mentioned above, CO binds hemoglobin 230-270 times more avidly than oxygen, so even small concentrations can result in significant levels of carboxyhemoglobin [1,2,3]. CO also binds myoglobin and has a high affinity for myoglobin, about 60 times greater than that of oxygen [4] resulting in cardiac depression and eventually hypotension. Consequently CO causes impaired oxygen delivery and thus utilization at the cellular level an affects several different sites within the body mostly the lung, heart, peripheral and central nervous system. Primarily, an intoxication with CO results in hypoxia and relative functional anemia. As stated earlier, the clinical picture often does not reflect the amount of COHb but in severe case, centeral nervous system will be affected leading to coma or even death if untreated.

3. EPIDEMIOLOGY, PREVENTION AND PUBLIC HEALTH

Carbon monoxide intoxications must be always highly suspected after burns. They are frequent and can lead to high morbidity and mortality. According to the literature, carbon monoxide poisoning is the most common cause of injury and death due to poisoning worldwide [5]. It has been estimated that more than 40,000 people per year seek medical attention due to carbon monoxide poisoning in the United States [6]. Sources of accidental CO exposure include heaters, fireplaces, kitchen, internal-combustion engines and many others. Prevention remains a vital public health issue, requiring public education on the safe operation in these fields, as well as increased emphasis on the installation of carbon monoxide detectors. In conclusion, fire protection methods are one of the most important aspects even considered being the main core because they decrease the incidence of burns and eventually the risk of having CO intoxication.

4. CLINICAL PICTURE

Carbon monoxide (CO) intoxication should generally be suspected after burns. CO is not easy to detect especially during the pre-hospital treatment. Furthermore, the clinical presentation of carbon monoxide intoxication can be overlooked.

Table 1. Symptoms and Signs at Varius Concentrations of Carboxyhemoglobin [36, 37, 38]

COHb %	Symptoms
0 – 10	None
10 - 20	Tightness over forehead, slight headache, dilatation of cutaneous blood vessels.
20 - 30	Headache and throbbing in temples.
30 - 40	Severe headache, weakness, dizziness, dimness of vision, nausea, vomiting, collapse.
40 - 50	As above; greater possibility of collapse, syncope, increased pulse and respiratory rate.
50 - 60	Syncope, increased pulse and respiratory rate, coma, intermittent convulsions, Cheyne-Stokes respiration.
60 - 70	Coma, intermittent convulsions, depressed cardiac and respiratory function, possible death.
70 - 80	Weak pulse, slow respirations, death within hours.
80 - 90	Death in less than one hour.
90 - 100	Death within minutes.

Medical courses of carbon monoxide intoxication can differ extremely [7] and as mentioned above, the clinical picture can be untypical and in many times is not related to the amount of COHb. The main manifestations of poisoning develop in the organ systems that depend on oxygen use such as the central nervous system and the heart [8]. Initial symptoms of acute carbon monoxide poisoning include headache, nausea, malaise, and fatigue [9]. Increasing of exposure can produce cardiac abnormalities including fast heart rate, low blood, and cardiac arrhythmia [10,11]. Central nervous system symptoms can also develop such as delirium, hallucinations, dizziness, unsteady gait, confusion, seizures, central nervous system depression, unconsciousness and respiratory arrest [12,13]. In severe cases, CO intoxication can lead to coma or even death. Some authors have stated that symptoms can differ according to the amount of COHb (table 1) [36,37,38]. Many authors have studied the relations between neurological symptoms and CO exposure time; no direct correlations between these factors have been found so far [14].

5. INVESTIGATION AND DIAGNOSIS

A history of potential carbon monoxide exposure should be confirmed, such as being exposed to a residential fire. The diagnosis is confirmed easily by measuring the levels of carbon monoxide in the blood. This can be determined by measuring the amount of carboxyhemoglobin compared to the amount of hemoglobin in the blood. Arterial blood gas (ABG) is one of the most reliable Investigations to detect the level of COHb. The non-invasive SpCO analysis using pulse CO oximetry (e.g. Rad57, Masimo Corp,USA) represents an easy device to diagnose CO intoxication. Pulse CO-oximetry is now available but still requires a special unit. The ratio of carboxyhemoglobin to hemoglobin molecules in a wealthy person is up to 5%, although heavy smokers may have levels up to 9% [15]. Myocardial ischemia is frequently associated with moderate-to-severe CO exposure [16]. Thus,

measurement of Troponin, creatinine kinase-MB fraction and myoglobin is essential especially in those patients who have cardiovascular history. Routine investigations should be also carried out including complete blood count, urea and electrolyte, liver function test as well as glucose level. Lactic acidosis is frequently observed in clinical CO poisoning [17, 18, 19]. Recently, it is suggested that the lactate level may be a useful prognostic factor, but this is still controversially discussed [20]. Furthermore, it was reported that plasma lactate is mildly elevated in pure CO-exposed patients. However, this mild elevation and the extensive overlap between the groups of neurological impairment severity do not suggest the usefulness of systematic plasma lactate measurement in pure CO poisoning [21]. It was also reported that the Glasgow coma scale and laboratory markers, such as white blood cells count and CRP serum concentration, are adequate additional tools with high potential for evaluating the severity of CO-related illness. Furthermore, Grieb et al. stated that COHb alone is an insufficient diagnostic tool for this purpose [22].

Fiberoptic bronchoscopy is by far an important tool for diagnosis and even treatment of inhalation injury. It identifies the degree of erythema, edema and ulceration. Thus, it is useful in evaluating the extent of injury. It can also be used to facilitate endotracheal tube insertion. Bronchoscopy is more sensitive and accurate than clinical examination in diagnosing inhalation injury and can even help to remove any necrotic cells and to perform toilet with suctioning.

Chest radiography should be performed in all case, although normal findings occur in many cases. CT scan can be done in severe cases especially those cases with neurological abnormalities, to identify for example cerebral edema or any focal lesion. In one study, 53% of patients hospitalized for acute CO intoxication had abnormal CT scan findings; all of these patients had neurologic sequelae. Of those patients with negative scan results, only 11% had neurologic sequelae [23].

6. TREATMENT

6.1. Pre-Hhospital Treatment

An immediate supply of high dose oxygen is essential to reduce mortality and long-term morbidity. Primary survey should be performed immediately for all cases of carbon monoxide intoxication after burn including assessment of airway, breathing, circulation and disability. Intubation for comatose patients must be performed in order to protect the airway. An important part of the acute treatment includes cardiac monitoring, pulse oximetry if possible, and vital parameters, although these values are not useful to detect COHb but still important. Blood sample may provide much more accurate correlation between COHb and clinical status in this phase.

Oxygen supply shortens the half life of carbon monoxide from 320 minutes to 80 minutes on normal air [24]. Herein, Oxygen increases the dissociation of carbon monoxide, thus turning it back into hemoglobin [25, 26]. CO intoxication has possible severe effects in the fetus; thus pregnant women are treated with oxygen for longer periods of time [27].

Table 2. Targeted arterial blood gas goals [39]

PH	7.25–7.45
PaO2	55–80 mmHg or SaO2 of 88–95%
PaCO2	35–55 mmHg (permissive hypercapnia can be used if pH _ 7.25)

6.2. Treatment in the Emergency Room

Treatment of carbon monoxide intoxication after burns is dependent upon the several factors including, severity of burns, and degree of inhalation injury, rescue time and the mode of treatment before transferring the patient to the hospital. Cardiac monitor should be performed immediately while receiving the case in the ER. Assessment of the airways is always essential and in some cases, immediate intubation is required. Direct laryngoscopy and fiberoptic bronchoscopy could be used to evaluate the extent of airway edema and burns. Breathing process should be checked to ensure the administration of 100% oxygen. Severe burns cause loss of fluids and electrolytes and may have a relevant effect on the circulation. Thus, circulation should be monitored to ensure the balance of the hemodynamic status. This includes replacement of fluids, electrolytes, and protein requirements. Central venous line may be needed to facilitate fluid resuscitation. Fluid resuscitation can be calculated by the Parkland formula. Administration of intravenousi.v- fluids is an important aspect to maintain the euvolemic state and to ensure adequate tissue perfusion. It is important to evaluate nutritional needs of burn patients because good nutritional support increases the healing process.

A new bedside pulse CO-oximetry is now available but it is not applicable in all centers [28]. Immediate transfer to a hyperbaric facility is considered for patients with levels above 15%, cardiovascular or neurologic impairment.

Aggressive treatment of acidosis with a pH above 7.15 is not recommended because it results in a rightward shift in the oxyhemoglobin dissociation curve, increasing tissue oxygen availability. Acidosis generally improves with oxygen therapy. As mentioned above, intubation can be conducted in case of sever inhalation injury.

6.3. Inpatient Care

Admission to the ICU is considered to evaluate acid-base status if COHb levels are 30-40% or above 15% with associated symptoms. COHb levels should be routinely measured to reflect the medical status of the patient providing an impression about the prognosis of the disease. Interdisciplinary approach is an important part of the treatment involving burn surgeons, neurologists, cardiologists. Neurological assessment requires more attention, thus other treatment plan can occur in order to stabilize the neurological status.

6.4. Hyperbaric Oxygen (HBO)

The philosophy of this kind of treatment is that the patient simply breaths 100% oxygen under increased atmospheric pressure. The first well-known chamber was built by a British priest named Henshaw. He built a structure called the domicilium that was used to treat a plenty of diseases [29]. The French surgeon Fontaine continued the idea of treating patients under increased pressure by building a pressurized and mobile operating room in 1879 [30]. Currently, HBO is standardized in many centers around the globe. On the other hand, the benefit of HBO treatment is still under current debate. Increased elimination of COHb clearly occurs and certain studies stated major reductions in delayed neurologic sequelae, cerebral edema, pathologic and central nervous system changes [31]. During the treatment with HBO, oxygen competitively displaces CO from hemoglobin. While breathing room air, this process takes about 300 minutes. While supplying 100% oxygen, this time is reduced to about 90 minutes. Treatment with HBO reduces this time to 32 minutes. Transferring a patient with CO intoxication after burns to a HBO unit is still a debatable issue. HBO should be highly considered for those who present symptoms with morbidity and mortality risks that include pregnancy and cardiovascular dysfunction and those who manifest unconsciousness neurologic signs or severe acidosis [32].

Complications of HBO therapy include decompression sickness, tension pneumothorax, gas embolism, reversible visual refractive changes and sinus or middle ear barotraumas. It was recently reported that middle ear barotrauma induced by HBO occurred in 13.6% of the patients. There was also no difference in incidence when comparing intubated and non-intubated patients [33]. Cortical blindness secondary to carbon monoxide poisoning, was even reported. [34]. In 2009, a case was reported from Taiwan stating the Damage of cerebellar white matter due to carbon monoxide poisoning [35].

7. SPECIAL CONSIDERATION FOR CHILDREN

Attention should be considered for burned children even without signs of carbon monoxide intoxication. The symptomatic child with any signs of respiratory distress and concurrent burns is admitted to the hospital for appropriate monitoring because edema and obstruction typically worsen over the next 24-48 hours.

Assessment of the airways is essential in any case to provide a normal path for the child. Clinical experience plays an important role in this topic especially with infants. Direct laryngoscopy and fiberoptic bronchoscopy could be used to evaluate the extent of airway edema and burns, although edema may appear later in several cases. Thus, intubation could be easily performed especially in the first 24 hours. Like adults, breathing process should be checked to ensure the administration of 100% oxygen. The affect of inhalation injury could be seen after 24 hours but this role cannot be applied in all cases. Severe burns cause ongoing circulatory derangement. Thus, circulation should be controlled to ensure the balance of the hemodynamic status. This includes replacement of fluids, electrolytes, and protein requirements. Central venous line may be needed to facilitate fluid resuscitation. Continuous evaluation of the blood pressure, oxygen saturation and temperature are needed to determine

the stability of such cases. The neurologic examination is frequently used but could be not specific especially if associated with severe hypoxia.

Regarding medications, corticosteroids are effective against inflammation and edema. However, no direct evidence exists for the use of steroids in carbon monoxide intoxication. Furthermore, steroids increase the risk of infections and delays wound healing. Antimicrobial therapy is reserved for patients with microbiologic evidence. The most common organisms are Staphylococcus aureus and Pseudomonas aeruginosa.

8. Special Consideration for Pregnant Women

A pregnant woman with carbon monoxide intoxication should be admitted immediately and receive a special care. Carbon monoxide can easily enter to the fetal circulation and COHb begins to appear. Pamela et al. stated that the affinity of CO to fetal hemoglobin (HbF) is even higher than to adult hemoglobin (HbA). Furthermore, a high amount of COHb causes hypoxia and consequently increases the risk of prematurity. Acute maternal intoxication may even result in fetal death. Treatment is not easy to conduct without a good evaluation. Therefore, these patients should have a multidisciplinary approach involving burns specialists, pulmonologists and obstetricians. Further follow up should be performed before discharge to ensure the safety of the mother and the developing fetus.

9. Prognosis

Carbon monoxide intoxication can be associated with high morbidity and mortality, involving multiple organ systems. This includes cardiac tissue, lungs, peripheral and central nervous system. Prognosis is mainly related to the affected system but also can be related to many factors which include the initial mode of treatment and elimination of the COHb. Patients can be discharged once they have no symptoms and levels of COHb below than 10 %. Further follow up is extremely recommended involving a pulmonologist, neurologist, psychiatrist and burn specialist.

Conclusion

Carbon monoxide (CO) intoxications are frequent and can lead to high morbidity and mortality, involving multiple organ systems (e.g. lung, heart, peripheral and central nervous system) and undetected CO exposure can be fatal. Carbon monoxide poisoning is the most common cause of injury and death due to poisoning worldwide [5]. Prevention remains a vital public health issue, requiring public education on the safe operation in these fields, as well as increased emphasis on the installation of carbon monoxide detectors. CO binds hemoglobin 230-270 times more avidly than oxygen, so even small concentrations can result in significant levels of carboxyhemoglobin [1, 2, 3]. CO intoxication should be always suspected after burns. Especially during the pre-hospital treatment, the clinical presentation of carbon monoxide intoxication can be overlooked. Initial symptoms of acute carbon monoxide

poisoning include headache, nausea, malaise, and fatigue [9]. Increasing exposure produces cardiac abnormalities which can include fast heart rate, low blood, and cardiac arrhythmia [10,11]. Central nervous system symptoms include delirium, hallucinations, dizziness, unsteady gait, confusion and coma. Arterial blood gas (ABG) is one of the most reliable investigations to detect the level of COHb. Furthermore, measurement of troponin, creatinine kinase-MB fraction and myoglobin is essential especially in those patients who have preexisting cardiovascular history. Glasgow coma scale and laboratory markers, such as white blood cells count and CRP serum concentration, may be adequate additional tools with high potential for evaluating the severity of CO-related illness. Furthermore, fiberoptic bronchoscopy is an important tool for diagnosis and even treatment. It identifies the degree of erythema, edema and ulceration. Bronchoscopy can even help to remove any necrotic cells and to perform toilet with suctioning. An immediate supply of high dose oxygen is essential to reduce mortality and long-term morbidity. Administering oxygen shortens the half life of carbon monoxide from 320 minutes to 80 minutes on normal air [24]. Treatment of carbon monoxide intoxication after burns is dependent upon the several factors including, severity of burns, and degree of inhalation injury, rescue time and the mode of treatment before transferring the patient to the hospital. Several steps should be conducted such as assessment of the airway, breathing and circulation. Fluid loss occurs in most cases after burns. Thus, it is essential to replace fluids by using the Parkland formula and control electrolytes level in the blood. Admission to the ICU is considered to evaluate acid-base status if COHb levels are 30-40% or above 15% with associated symptoms. Patients with neurological symptoms such as cerebral edema may be transferred to the neurosurgical intensive care unit.

Hyperbaric oxygen therapy is standardized in many centers around the globe. On the other hand, the benefit of HBO treatment is still under current debate. Complications of HBO therapy include decompression sickness, tension pneumothorax, gas embolism, reversible visual refractive changes and sinus or middle ear barotraumas. It was recently reported that middle ear barotrauma induced by HBO occurred in 13.6% of the patients. Attention should be considered for burned children even without signs of carbon monoxide intoxication. The symptomatic child with any signs of respiratory distress and concurrent burns should be admitted to the hospital for appropriate monitoring because edema and obstruction typically worsen over the next 24-48 hours. A pregnant woman with carbon monoxide intoxication should be admitted immediately and receive a special care. Furthermore, a high amount of COHb causes hypoxia and consequently increases the risk of prematurity. Acute maternal intoxication may even result in fetal death. Herein, prognosis is mainly related to the affected system but also can be related to many factors which include the initial mode of treatment and elimination of the COHb. Further follow up is extremely recommended involving a pulmonologist, neurologist, psychiatrist and burn specialist.

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Chapter 10

LITERATURE REVIEW AND CLINIMETRICS ASSESSMENT OF THE LASER DOPPLER IMAGING IN BURNS DEPTH ESTIMATION

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ABSTRACT

Burns depth assessment in the early stage of burn injury is a crucial point in determining the need for an early surgical intervention. It is very important to accurately assess the burns depth as early as possible and decide whether these are superficial and will heal spontaneously or deeper and warrant earlier excision and grafting. Traditionally, visual and tactile assessment is an easy, fast and non-invasive method (Sainsbury 2008). Such method is considered to be subjective and sometimes inaccurate. The ideal method should be non-invasive, cheap and easy to use, have minimal risks and side effects and most importantly to reliably predict healing chance and time with estimation of scar risk formation (Black et al. 1986). This assignment will examine the effectiveness of the Laser Doppler Image (LDI) in assessing burns depth in the early stages after the injury. This will be through literature search of related studies as well as assessing this tool's potentials using the concept of clinimetrics. It is a methodological discipline concentrating on clinical measurement quality. It is essential to examine a new instrument's clinimetrics properties before applying it in clinical practice. The LDI as a tool for burns depth assessment seems to show high validity, reliability, reproducibility, responsiveness and acceptability, further prospective studies are important to re-assess this tool and its clinimetrics. A clear understanding of the limitations of LDI is needed to put the current research in perspective to find the right clinical application for LDI.

INTRODUCTION

Burns depth assessment in the early stage of burn injury is a crucial point in determining the need for an early surgical intervention (Wexman et al. 1989). It is very important to

accurately assess the burns depth as early as possible and decide whether these are superficial and will heal spontaneously or deeper and warrant earlier excision and grafting. Traditionally, visual and tactile assessment is an easy, fast and non-invasive method (Sainsbury 2008). Such method is considered to be subjective and sometimes inaccurate; with experienced burn surgeons being able to accurately assess the burns depth clinically in 64-76 % of cases (Jaskille et al. 2010). Histological examination is considered the 'gold standard' (Kahn et al. 1979, Ho-Asjoe et al. 1999). However, this is a painful and invasive method and therefore alternative non-invasive methods have been sought. None of these methods proved to be consistently reliable; this included the 'India Ink' injection, ultrasound and flowmetry (Wexman et al. 1989). The ideal method should be non-invasive, cheap and easy to use, have minimal risks and side effects and most importantly to reliably predict healing chance and time with estimation of scar risk formation (Black et al. 1986).

This assignment will examine the effectiveness of the Laser Doppler Image (LDI) in assessing burns depth in the early stages after the injury. This will be through literature search of related articles and studies as well as assessing this tool's potentials using the concept of clinimetrics. The concept of clinimetrics was introduced by Feinstein (De Vet et al. 2003). It is a methodological discipline concentrating on clinical measurement quality. It is essential to examine a new instrument's clinimetrics properties before applying it in clinical practice.

LASER DOPPLER IMAGING (LDI)

The Laser Doppler technique was first described by Stem (1975) for assessing skin microcirculation. In the older version, the Laser Doppler Flowmetry (LDF), the backscattered signal is transferred into an electrical signal, and after being processed, the outlet voltage will correlate linearly with skin perfusion (Mandal 2006). LDF was first used by Micheels et al. (1984) for clinical assessment of burns depth and they suggested its ability to define different degrees of burns. Recent advances introduced the Laser Doppler Image (LDI). A machine in which a red light is directed onto the affected area, which is reflected back into machine and received by a photo detector, which can differentiate between amount of light reflected by static tissue (indicating absence of circulation in that area and subsequently a deeper burn) and that reflected by circulating objects (red blood cells indicating positive perfusion and subsequently a more superficial burn). The technology provides an estimate of perfusion through the burn wound (measured by ml/g/min). The assumption being that lower perfusion correlates with deeper burns and, therefore, less healing potential, and vice versa.

VALIDITY

A measure is valid if it really measures what it is supposed to measure (Streiner and Norman 1995). They suggested that criterion validity is the most powerful subtype of validity and defined it as the ability of instrument to give results that match the gold standards (histology biopsy in the case of burns depth assessment). Predictive validity is used whenever tests are used to predict how an individual will perform in the future based on a measured variable today.

Green et al. (1988) examined patients 72 hours post acute burn injury using LDI to assess the skin perfusion in partial thickness burns, as well as in experimental rats with similar size burns (relatively to their total body surface area). They concluded that wounds that showed constantly high perfusion levels healed without grafting, while wounds that showed lower perfusion levels eventually required grafting. The important result was that the differences between average flow levels for healing and non-healing burns were statistically significant. O'Reilly et al. (1989) examined 59 acute burns in 41 patients. They found a positive predictive value of 98.4% using the LDI, whereas the clinical estimation did not correlate as well with the depth of injury. Waxman et al. (1989) studied 33 patients with 51 burns and assessed them in the first 48 hours after the injury. They included only burns of intermediate depth according to clinical assessment by experienced burns nursing staff and surgeons. The study predicted healing with 100% specificity in burns with LDI reading > 6 ml/g/min, and predicted non-healing with 75% specificity for reading < 6 ml/g/min. These predictive values slightly changed as the temperature of the probe was changed.

These studies did not comment on the general status of the patient or the burn during the 3 weeks period; for example, whether the patient was generally unwell or if there were infective complications of these burns during this period, both of which would affect the burns potential for healing and bias the doppler results interpretation, and as a result, these burns should have been excluded.

Niazi and colleagues (1993) studied 13 patients and assessed the burns depth using clinical assessment, LDI and punch biopsies. They reported statistically significant (P) correlation between the LDI and biopsy results. Comparing the clinical assessment with histology results showed only 41% accuracy, with 17 % of burns being clinically over diagnosed (thought to be deeper, though histology assessed them to be more superficial) and 17% were under diagnosed (clinically thought to be more superficial, though histology confirmed them to be deeper). Correlation between clinical assessment and LDI showed to be accurate in 77% of the cases, with 15 % being over diagnosed clinically and 7% being under diagnosed clinically. This is one of few studies that compared the LDI to the gold standard histological biopsies. The main issue with this study is the small sample size; although they collected patients over 21 months with 347 admissions, they included only 13 patients.

Atiles et al. (1995) reported a 100% positive predictive value of 100% for non-healing wounds on post burn days 1 and 3 in adult patients. Further work by Yeong et al. (1996) on paediatric burns suggested a 94% accuracy in prediction of burn wound healing time compared with physician predictive accuracy of 70%. Unfortunately, none of them compared the LDI to histology results.

Brown et al. (1998) used large white pigs and inflicted their skin with chemical burns and compared the LDI results to histological results. They reported the LDI to significantly correlate well with histo-pathological assessment. Although it is known that it is hard to transfer research data and results from animals to humans, previous researches have suggested pigs as the best model for studying human skin wound healing due to the similarity anatomically and physiologically (Sullivan et al. 2001).

Pape et al. (2001) assessed 48 patients with 76 intermediate depth burns. 43 burns were diagnosed to be superficial by the LDI and were treated conservatively with dressings, of which 41 (95%) healed within 21 days, the other two burns were complicated by infection and healed within 28 days. Clinical judgement was accurate in 30 out of the 43 burns (69%). LDI identified low perfusion (deeper burns) in 25 of the 76 burns, which were treated

surgically, with a 100% agreement with histology, whereas clinical judgement reached only 84% concurrence with histology. Most importantly, Chatterjee (2006) assumed that this study's interval validity is minimized as the authors used two outcomes; they followed the assumed superficial burns (by the LDI) 21 days to decide their superficiality upon healing, on the other hand, they biopsied the assumed deeper ones earlier in the study as they were diagnosed by the LDI.

Jeng et al. (2003) compared LDI with clinical examination in a prospective blinded trial of 23 patients with 41 burns The surgeons accurately determined the depth in 71% of the cases, while the LDI accuracy was 100%. However, as only 21 wounds underwent histological analysis (all deemed clinically to be deep burns), this only offers construct validity which means the degree to which scores on an instrument relate to other measures in a manner that correlates with theoretically-derived hypotheses concerning the constructs being assessed (Dekker et al. 2005). Monstrey et al. (2001) presented similar results to Jeng and colleagues; showing the accuracy of the LDI to be 100%.

SENSITIVITY AND SPECIFICITY

Sensitivity, which with respect to the LDI is the ability to correctly identify deep burns, as well as specificity, which is the ability to correctly identify superficial burns, are both indicators of the instrument validity (Margolis et al. 1996). LDI specificity ranged between 92 to 97% and sensitivity between 90% to 100% according to many studies (Pape et al. 2001, Holland et al. 2002, La-Hei et. al. 2006 Mcgill et al. 2007). There are two main issues with these studies. First, the LDI was examined in comparison to clinical assessment of burns, rather than the gold standard histology biopsy. Second, as LDI has been reported to be accurate only down 2 mm skin depth (Mcgill et al. 2007), and it has been reported that skin of the soles and the palms can reach up to 4 mm, the specificity and the sensitivity of these studies may be affected as none of these studies reported exact sites of the burn areas studied. One potential area for bias in using the LDI is the fact that the operator can clinically assess the burn depth judging on the capillary refill as well as pain and tactile sensation while performing the scan, which can potentially affect their clinical judgement. Some interesting work by La-Hei et al. (2006) was performed to overcome this problem. They allowed the investigators to view the LDI scans and see photographs of the burn areas they scanned and comment on them. This indeed reduces the bias caused by the investigator's clinical assessment of burns depth depending on capillary refill and sensation-pain elements, though; it will still cause bias by viewing the photographs, which will again help the investigators to clinically assess the burns depth. In this study, the LDI still scored specificity of 95% and sensitivity of 100%. Again, as with previous studies, this as measured against clinical assessment rather than histological diagnosis.

REPRODUCIBILITY

Reproducibility encompasses reliability and agreement; a test is considered reliable if it always produces the same results under the same conditions, conversely, agreement is the

lack of measurement errors (De Vet et al. 2003). Most studies presented above scanned the burns only on one occasion, usually 48-72 hours after the burn injury as previously identified by authors to be the most sensitive and specific time for their assessment.

Niazi et al. (1993) concluded that the LDI showed test-retest reliability and was consistent with burn wound assessment methods at day one, two and three post injury. However, the sample size was small (only 13 patients) and measured this against clinical assessment. These results were still supported ten years later by Jeng et al. (2003) by performing daily scans on the burns and results being consistent with conventional clinical assessment. Jeng et al. (2003) scanned these burns daily for the first 5 days post burn injury and concluded that the LDI gave consistent results, even though the scan were performed by different operators. Interestingly, the clinical assessment varied from day to day, and that shows its poor reproducibility and as a result signifies the problem with studies that assessed the LDI's validity in comparison to clinical assessment which showed poor reproducibility.

Monstrey et al. (2001) doubted the reliability of the LDI in the first two days after burn injury, and believed it improved substantially between days 3 and 6 (93–96.% with LDI versus 61–67% with clinical evaluation alone). This may why different authors decided to choose to assess the burn 36-72 hours after the burn injury, though explanation has been missing from all these papers.

One important issue to point out in assessing the clinimetrics of the LDI is the fact that different body parts have different baseline perfusion. For example, Allely et al. (2008) study on elective normal volunteers found higher perfusion in the nose (525 perfusion units) compared to the forehead (280 perfusion units). What effect, if any, this difference can play in a burn patient is unknown. This may potentially affect the results of the scans assessing the burns depth as the scan assesses perfusion depending on a generic value for a specific patient. Most studies presented above did not use controls; an important factor that can affect their reliability and the validity.

RESPONSIVENESS

Responsiveness is important if a measurement instrument is required to detect change over time (De Vet et al. 2003). Monstrey et al. (2001) suggested the ability of the scans to detect changes of burns depth with time. This was further supported Jeng et al. (2003) who suggested that the LDI scan results improved with repeated scanning. However, it is debatable whether the repeated scans is of any clinical importance as a scan performed at 48-72 hours after burn injury is sufficient for depth assessment and implement a decision whether to allow healing or treat surgically with excision and grafting. This makes the need for repeated scanning is controversial; as this would not change the decision already made on scanning the burn in the first 48-72 hours.

INTERPRETABILITY

Interpretability is the extent to which meaning may be assigned to quantitative scores (Dekker et al. 2005). Information is required on the clinical meaning of scores and which

differences between scores can be regarded as clinically meaningful. Information on minimally important clinical differences or that allows scores to be interpreted is a positive attribute (Dekker et al. 2005). LDI gives colour-coded map which correlates to a median flux value. These images and values can be easily interpreted, but this needs basic training and is subjected to a learning curve (La-Hei et al. 2006).

ACCEPTABILITY

Acceptability means a test must be suitable for the target population to allow it for a widespread use. For burn depth assessment, the population will include patients of a wide range of ages. Holland et al. (2002) investigated the use of LDI in paediatrics (less than 16 years of age) and concluded that they tolerated it well; with only 1 patient out of 57 needing sedation for scanning. They also concluded that these scans were accurate despite the child moving during the test.

A major disadvantage of the scanning beam in LDI devices is their slow scanning speed, leading to patient discomfort and imaging artefacts (Van Herpt al. 2010). Also, patient mobility (breathing and shivering) affect the results (Jaskille et al. 2010). Most of the studies presented have examined a specific population with a limited number of patients (less than 50 in most of them). Also, these studies have used different makes of the machines with different scanning distances on different body parts, which make comparisons between studies and broad conclusions difficult to conclude.

COST

LDI machines, including PC and software, cost approximately £35,000 (Sainsbury 2008). Jeng et al. (2003) reported that the LDI reduces the hospital stay by 2 days by providing earlier assessment and decision making for burn management.

CONCLUSION

LDI is non-invasive, relatively easy to mobilise and utilize and without risk. The only requirement not met is being relatively expensive.

Studies presented above showed the LDI to have sensitivity of 90-100% and specificity of 92-97%. The LDI shows criterion validity when compared with the gold standard assessment (histological biopsies) and can help to expedite burns management and optimise the use of available resources.

Although the LDI as a tool for burns depth assessment seems to show high validity, reliability, reproducibility, responsiveness and acceptability, further prospective studies are important to re-assess this tool and its clinimetrics. This will substantially improve the quality of burns management when used as an adjunct tool to clinical assessment. It is unlikely that LDI will replace clinical assessment for burn injuries, but it is likely that it will become a standard method of assessment and may, in the long term, replace biopsy and histology as the

gold standard. A clear understanding of the limitations of LDI is needed to put the current research in perspective to find the right clinical application for LDI.

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Chapter 11

THE CLINICAL APPLICATION OF VERSAJET HYDROSURGERY SYSTEM™ IN BURN DEBRIDEMENT

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INTRODUCTION

The primary goal of acute burn management is debridement of necrotic skin and underlying tissue to expedite healing (Heimbach 1987, Soroff and Sasvary 1994, Eldad et al. 1998). Early debridement (within 2-3 weeks) is superior to late debridement for deeper burns that are unlikely to heal spontaneously (Cohen 1984, Davis et al. 1996). Heimbach (1987) suggested two types of burn excision. Tangential (sequential) excision removes nonviable sparing viable tissue, with an end point of punctuates bleeding judged by the surgeon. Excision down to fascia is used in large full-thickness burns when patient's mortality is the main concern against bleeding and long operative time.

The choice of the debridement method depends on many factors including burn depth, amount of slough, patient's condition and surgeon's experience. Jeffery (2007) suggested disadvantages of different methods. A guarded blade, such as Watson knife, remains an issue of depth perception and difficult to correctly apply to different body parts causing unnecessary debridement of healthy tissue and increased blood loss. Also, the ''shelving'' effect due to variances in excision slopes conflict with the uniform surface needed for reconstruction and the ''stuck on'' appearance due to excessive tissue at the periphery of the debrided area. Dermabrasion debridement using dermatomes and rotating burr or dermabrader allow more precise debridement reducing healthy tissue loss, but can be difficult to use due to increased bleeding. Ablative laser, such as CO2 laser, is rarely used because of practical limitations and it also leaves a thermally damaged layer (0.1 mm thick) on the surface (Green et al. 1992).

Although this water-jet dissection system has been used for more than two decades in liver, kidney and laparoscopic surgeries (Papachristou and Barters 1982, Shekarriz et al.

1999, Piek et al. 2002, Skekarriz et al. 2003), it was introduced only recently into wound debridement (Attinger et al. 2006) and burn debridement (Klein et al. 2005).

VERSAJET HYDROSURGERY SYSTEM™

A new instrument, the Versajet™ Hydrosurgery System (Smith and Nephew), utilizing the Venturi effect, has recently been introduced and specifically designed for controlled surgical debridement. It contains a power console that propels saline through a handheld cutting device with the resulting vapour of pressurised saline working as a knife along the operating window. Simultaneously, the debrided tissue is aspirated into the suction receptacle. The hand-piece is available with either an 8-mm or 14-mm operating window and with either a 45- or 15-degree angle (14-mm hand-piece only). The cutting power can be adjusted to permit different cutting powers (graded 1 to 10), making it more facile, precise and haemostatic. This allows skin appendages critical for timely re-epilialisation and sensitive tissue preservation. Also it is an important tool when debriding over important underlying structures, such as tendons, cartilage and bone, in challenging convex and concave areas, awkward areas hard to get into and areas of very thin skin, such as eyelids and genitalia.

LITERATURE REVIEW

Klein and colleagues (2005) reported their personal experience using Versajet™ in debridement of burn eschar in challenging body areas (scalp, eyelids, ears, lips, palm, digits, web spaces, periareolar and toes) in 44 patients (adults and paediatrics). They claimed no patients required repeat grafting as the result of inadequate excision, and no patients had graft loss as the result of excessive tissue excision. It is not clear what they meant by this result; as they may mean there were patients requiring re-grafting and others with graft loss, but none is due to Versajet™ debridement failure. The sample included 44 patients over 2-3 years, with no specification of inclusion and exclusion criteria. Multiple surgeons operating on the sample makes it more representative of normal practice and demonstrates reliability; resulting from different experiences and operating skills.

Rennekampff et al. (2006) used Versajet™ on 17 patients (1 paediatric and 16 adults) with acute burn injuries ranging (0.5-40%) total body surface area (TBSA) on face, hand, leg and foot. All burns were covered with biosynthetic dressings (Biobrane™ and TransCyte™, Smith and Nephew) and/or skin graft, depending on burn thickness. The three groups (superficial, intermediate and deep burns) were homogenous for this post-debridement coverage; 3 superficial partial-thickness: (n=1 Biobrane™, n=2 Biobrane™ and skin graft), 8 intermediate partial-thickness: (n=4 Biobrane, n=1 Biobrane™ and skin graft, n=3 skin graft) and 6 deep partial-thickness: (n=1 Biobrane with skin graft, n=5 skin graft). They reported that the skin grafts result was comparable to that obtained with standard debridement techniques. There was a degree of consistency in post-debridement dressing coverage within each group, which reduces the contamination in outcome results. They claimed that all cases healed appropriately with no complications, which reflects the efficacy of Versajet™. This is

a subjective assessment; they should have used objective parameters, such as healing time and percentage of graft take. The sample was small with no control group.

Cubison et al. (2006) reported their experience using Versajet™ in paediatric burns as being very effective at cleansing and debriding superficial and intermediate burns prior to biosynthetic dressing (Biobrane™ or TransCyte™) application and debriding deep dermal burns prior to skin grafting. Their sample included 7 children with ages (10 months - 6 years) and acute burn injury of different sites and sizes (1-12% TBSA). Six out of seven cases healed completely with either grafting or biosynthetic dressings. Five cases healed with no hypertrophic scarring and 1 with slight scarring. In 1 case, where the burn was very deep as confirmed by Lased Doppler Image (LDI), they reverted to conventional knife excision to allow a smoother wound bed. They also claimed that Versajet™ allowed biological dressings to be used beyond 24 hours after injury (which is the usual time frame to use biosynthetic dressings), but will not convert unsuitable burn into a suitable one. Interestingly, they performed LDI immediately following Versajet™ debridement, which showed that Versatjet™ did not interfere with burn depth assessment and showed no increased blood flow at the periphery of the burn, concluding that Versajet™ does not provoke an immediate inflammatory response in normal skin. Also, they reported particular advantage by debriding over-granulating areas adjacent or within mesh of recently healed graft. As with many similar studies, the sample was small, with no details regarding patients' selection and no control group.

Tenenhaus et al. (2007) examined 13 adults with intermediate-deep partial-thickness thermal burns to the face and neck ranging 3-5% TBSA at two burn centres (USA and Germany) over a period of 3 years. All burns were debrided with Versajet™ and managed with biosynthetic dressings. All cases healed within a period of 8-19 days and no complications (including the need for scar revision). Two cases needed split thickness skin grafting and healed completely. The sample size was small, especially when considering such a long period, and lacked a control group. A particular advantage of this study is using the same coverage for all debrided burns (biosynthetic dressings). They claimed that the approach to such injury is justifiable and should be thoroughly investigated.

Gravante et al. (2007a) examined 20 patients over a period of 30 days. Thirteen patients were operated on for the first time and seven had previously been operated on with conventional debridement and skin grafting and needed further excision of small infected necrotic areas. This study described their personal experience, with no objective assessment of outcomes. They claimed the amount of blood loss was similar to that of knife debridement, though no evidence was provided. Interestingly, they were the first to claim that Versajet™ debridement was even faster than conventional methods of eschar excision. They stated that the system was more accurate and precise than classic knife debridement, but less accurate than dermabrasion in reaching the correct viable plane and for this reason should not be used in children. Furthermore, during the first operation with Versajet™, the surgeon applied a moderately stronger pressure and this inadvertently cut a large subcutaneous vessel, which reflects a learning curve with the use of the system. Although there was no evidence to support their view, they excluded paediatric patients as it was too risky to begin with the delicate skin of children, for whom they used dermabrasion, as previously advocated by Esposito et al. (2006). It is indeed in this group with thinner skin and higher risk of hypertrophic scarring and contracture, the use of Versajet™ for precise excision is of particular importance. Kimble et al. (2008) challenged the suggestions to exclude paediatrics

Versajet™ a valuable tool to maximise dermal preservation prior to skin grafting in paediatricpatients. Fifty children with median age of 2.4 years and 5% mean TBSA were debrided by Versajet™ and grafted. They reported graft take of > 90% in all but one child (where it was 50%).

After their encouraging results, the same authors (Gravante et al. 2007b) conducted the first and currently only prospective randomised clinical trial in this field. They compared Versajet™ to their normal practice using the hand-held dermatome escharectomy in 87 adults debrided within 3 to 17 days post thermal deep-partial to full-thickness burns. The study sample was collected over a period of one year and recruited 87 out of the potential 100 patients (13 excluded were paediatrics or adults with high risk of prolonged anaesthesia). The study was single blinded; patients were blinded to treatment (being under general anaesthesia), while the surgical team were not. Both groups were homogenous for comorbidities, demographics and burn depth. Burn depth assessment was not mentioned. Both arms of the study received the same pre-operative disinfectant, intra-operative grafting technique and post-operative analgesia. Theatre visits for each patient ranged from 1 to 3 sessions depending on burn TBSA and presence of infection. The two primary endpoints were time needed for debridement and the efficacy of Versajet™ to reach the correct bloody dermal plane. The three secondary endpoints were analgesia effect, eventual adverse effects (cooling effect and bleeding risk) and contracture formation. Some of these outcomes were assessed subjectively according to clinical opinions of surgeons involved in the operations, whom were not blinded to the two interventions used. In their abstract, they claimed that Versajet™ was faster ($P<0.05$) and more precise in obtaining the correct plane. However, in their discussion, they stated that when the analysis was restricted to areas that required extra-attention (ie, hands, face, genitals), the Versajet™ system was shorter ($P=0.02$), whereas when restricted to large areas (trunk, arms, legs) it was significantly longer ($P =0.01$). Intra-operatively, they believed that Versajet™ was more accurate in obtaining the correct plane. Although the results showed better outcomes of Versajet™ compared to dermatome escharectomy for postoperative pain relief (evaluated with the visual analogue scale), adverse effects (cooling effect and bleeding risk, assessed intra-operatively by surgeons clinical judgement), healing times and contracture rates (evaluated clinically with a follow up visit after 6 months), all were not statistically significant ($P>0.05$). They believed that Versajet™ was easier to use, more precise and reduced hazards for the surgeon and the operating staff compared to debridement using sharp instruments. Although their exclusion of paediatric patients has been previously challenged by Jeffery (2007) and Kimble et al. (2008), they pointed that recent work by Cubison and colleague (2006) whodescribed the positive effects of Versajet™ on children.

A subsequent case series by Rees-Lee et al. (2008) concluded that the main indications for Versajet™ are cleansing of late-presentation paediatric scalds to allow the application of biological dressings (Biobrane™ and TransCyte™),dermal preservation in mid-dermal paediatric burns and burns in anatomically and aesthetically challenging areas. Their study included 10 patients (3 adults and 7 paediatrics) presenting with acute burns (9 thermal and 1 chemical) in different body areas with 3-17% TBSA. Two end points were evaluated. First, the healing potential, where 8/10 healed with no problems, with 2/10 needing further grafting. Second, the resulting scarring, where they used Vancouver Scar Scale (VSS) and claimed favourable scarring results, with the scar being managed with simple conservative scar therapy. VSS is a commonly used scar assessment scale that rates the scar on its appearance

to parameters such as vascularity, pigmentation and other parameters (Baryza and Baryza 1995). The sample was small, not randomised and did not include a control group. Different therapies following debridement were used, including biosynthetic dressings and/or skin grafting. These therapies were appropriate to burn size and depth and followed their standard protocol. They identified some disadvantages of the system; including being expensive, time consuming in large surface area (doubled compared to conventional methods), hypothermia, inaccurate deeper debridement at higher settings and technical issues.

Further personal experiences have continued to follow. Shafer et al. (2008) reported quick debridement of a hand burn with excellent graft take and aesthetic and functional outcomes. Yeh et al. (2010) reported their successful use of Versajet™ in total penile full thickness thermal burn and reconstruction with split thickness skin graft. They reported complete graft healing, no contracture or prominent scarring and patient's satisfaction aesthetically and functionally. Gumus et al. (2010) reported their satisfaction using Versajet™ in a 42-year-old man with a deep partial thickness chemical (hydrochloric acid) forearm burn. The burn was debrided on the day of injury and dressed with conventional vaseline gauze and healed completely without complications. Boudana et al. (2010) treated sulphur-mustard vesicant burn in a 47-year-old male that failed to heal by conventional debridement and grafting. Complete healing was reported after 2 weeks, soft and pliable scar at 1 month and no evidence of hypertrophy at 6 months. The patient was satisfied with the cosmetic results.

Two crucial points to mention about all presented studies. First, although they used clinical assessment for estimating burn depth -which is the commonly used method- it is only 60–80% accurate (depending on experience of the assessor) compared to more accurate methods, such as Laser Doppler Imaging (disadvantage being expense and availability) and tissue biopsy (disadvantage being invasive) (Pape et al. 2001, La Hei et al. 2006). Second, the authors reported that these burns were accurately debrided when punctate dermal capillary bleeding occurred.

Some precautions have to be taken in considerations when using this system. Cubison et al. (2006) noticed a cooling effect on their paediatric patients, but this was prevented by using warmed solutions for the machine. Also, they tried reducing blood loss by adding adrenaline to this solution, though they did not notice significant vasoconstriction effect. Rennekampff et al. (2006) claimed that they and other authors have found the Versajet™ system, in its present form, is inadequate for excision of full thickness and leathery dried eschars. They pointed that this instrument did not impose any additional risk to the operating room personnel caused by splash and splatter caused by conventional methods as well as minimizing exposure to yet another sharp cutting device on the field. Jeffery (2007) warned about the ''scalloping'' effect of the underlying fat when using this system for full thickness burns caused by the high-pressure fluid that will preferentially remove the softer tissue underneath the hard full thickness burn, and preferred the use of conventional blades for debriding these burns.

CONCLUSION

Versajet™ hydrosurgery debridement is reported by many authors to be an excellent tool in the debridement of mixed depth burns allowing dermal preservation and full thickness

burns in anatomically and aesthetically challenging areas. As with any piece of equipment, there is a learning curve associated with the tool for operators and nursing staff. It is supposed to be a short curve, with no dangerous complications if used cautiously. Debridement will take longer at first, but this will become faster with more experience, but may still be slightly slower than conventional methods. Being more expensive and time consuming compared to conventional methods, clear indications are needed for its use in acute burn debridement. Different studies have claimed that Versajet™ hydrosurgery may provide an efficient and cost-effective alternative to conventional surgical burn debridement. However, the evidence available is largely based on expert opinion. Most literature evidence is based on personal experiences and only one prospective randomised clinical trial. Such descriptive studies include the lack of control groups, selection bias and lack of blinding. Hence, these claims need to be interpreted cautiously. On the other hand, despite being personal experiences, these studies still represent a clear indication of the system's efficacy to justify larger studies and RCTs. Further work is encouraged to examine its efficacy and advantages as a useful adjunct in burn wound excision compared to conventional methods. This will assess surgeons to decide where and when to use it and result in valuable benefits on the patients' post-operative clinical, financial and psychological outcomes.

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Chapter 12

HOW TO PERFORM AN ESCHAROTOMY IN BURNS: INDICATION AND TECHNIQUE

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ABSTRACT

The initial treatment of burns is in most cases, performed by health care personnel not specialized or experienced in treating burns. In circumstances where rapid transportation to a burns center is not possible, such as in hostile environments but also in Western Europe and North America, there can be a vital indication to perform escharotomy during the first period of treatment at a primary hospital. The indications for escharotomy of the neck, upper and lower extremities, and the thoracic and abdominal wall are discussed. The proper operative technique and post-surgical treatment of these procedures are described.

Keywords: Escharotomy, burns, operative technique

INTRODUCTION

The principles of treating burn patients with an escharotomy have not changed much since the publication of Pruitt et al. in 1968 [1]. Nevertheless, these principles, in our experience, are often unknown, poorly taught and ineffectively performed.

Because patients with burns are almost always initially treated by health care workers not specialized or experienced in treating burn patients, it is important to know how to resuscitate and stabilize these patients. [2,3]

In addition to airway management, ventilatory therapy and fluid resuscitation, escharotomy is one of the few early operative interventions with a vital indication. Delay of

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this procedure can lead to ischemia of the extremity, distal from the burn wound, compromise airway and impair ventilation. In the Emergency Management of Severe Burns (EMSB ®) course and the Advanced Burn Live Support (ABLS®)course, indications and proper technique are taught and learned, but care providers still tend to lack this knowledge.

Because of the systemic effects and the dynamic behavior of a burn wound, especially in patients that require extensive fluid resuscitation, the need for an escharotomy can develop within the first 48 hours.

Even in Europe and North America, there may be circumstances in which a patient cannot be admitted to a specialized burn unit within the first few hours of the accident, e.g., in cases of a catastrophe with multiple victims. This limitation is also true for military circumstances elsewhere in the world, where limitations in transport capacity create the need for the intermediate treatment of patients during the first three to six days after an injury [4].

Thus, it is important for health care workers to be aware of the indications and technique for an escharotomy.

PATHOPHYSIOLOGY

Escharotomy is derived from the Greek word *eschara* which means: "crust."

When we commonly refer to an eschar, it always exclusively means the skin remnant of a full thickness burn, frostbite or skin damage by a corrosive chemical.

Thermal injury causes denaturizing of collagen and elastin in the dermis, resulting in shrinkage and loss of skin elasticity. In combination with an increase of tissue pressure caused by the hyper permeability of vessels and fluid resuscitation, the rigid eschar can act like a tourniquet in the extremities, especially in cases of a nearly circular burn wound, thus resulting in tissue ischemia and necrosis secondary to impaired perfusion.

INCIDENCE

There are almost no data to be found in literature that report the incidence of escharotomy. In our institution, one of the three burn centers in the Netherlands, escharotomies were performed in six percent of all burn patients admitted over the last 13 years.

INDICATION

An escharotomy can be indicated for the extremities, the neck or the trunk and can be necessary as a preventative or therapeutic measure.

- *Prophylactic escharotomy of an extremity* is advised in cases of a circular or near circular full thickness burn wound in the upper or lower extremity, especially when a prolonged transportation time is expected (greater than 4 hours) or when there is limited perfusion monitoring of the affected extremity.

- *A therapeutic escharotomy of the extremity* must be performed in the presence of the following symptoms of perfusion impairment:
- paleness
- pain not related to the injury
- paresis of the extremity that is distal to the burns
- pulselessness of a distal artery(radial artery, dorsal tibial artery, dorsal foot artery)
- delay in capillary refill.

Monitoring oxygen saturation with pulse oximetry can be helpful.

The interpretation of these signs, however, can be difficult in the presence of burned skin or in circumstances of hypothermia and hypovolemia, each of which make it difficult to feel for pulses or control the capillary refill. In these cases, Doppler ultrasound can be helpful. [5]

One must realize that an impairment of arterial pulses and diminishing Doppler signals signify late symptoms of poor perfusion.

- Escharoromy of the neck is indicated in cases of a circular or nearly circular full thickness burn of the neck region, especially the anterior portion. The post-burn edema, in combination with a rigid eschar, can compromise soft tissue and the airway, even in intubated patients.
- A full thickness burn of the anterior thoracic wall continuous with the lateral side of the body or abdominal wall can cause impairment of the necessary thoracic movements for ventilation, even if the back is not affected.

Important signs are hypoventilation due to decreased thoracic wall compliance resulting in anoxia and, in case of mechanical ventilation, a high ventilation pressure.

- Full thickness burns of the abdominal wall alone or in combination with an involved thoracic wall can lead to intra-abdominal hypertension(IAH) and abdominal compartment syndrome. (ACS) Fluid overload during resuscitation will increase this risk [6] According to international guidelines, abdominal hypertension is defined as an intra- abdominal pressure of 12 mm Hg or more, and abdominal compartment syndrome is defined as an intra- abdominal pressure of 20 mm Hg or more with proven organ failure. [7]

The incidence of IAH and ACS in burns is not known because most studies reporting incidence data were published before a concensus was established for their definition. Percentages vary from 1.8% to 70 %, depending on the burn TBSA and patient group studied. [8,9,10,11,12] Measurement of the intra-abdominal pressure is important from the initiation of treatment, not only when organ function impairment is recognized. [13,14]

TECHNIQUE

In general, an escharotomy must be performed as a sterile procedure in a hospital and not immediately at the scene of an incident.

Although we strongly recommend performing the operation under general anesthesia in children, this is not always required in adults. However, good sedation and analgesic medications are needed, despite the fact that full thickness burns are generally insensate. All escharotomies, not only in the extremities but also in the neck and the trunc must be performed bilaterally.

To minimize blood loss, the incisions are preferably performed with electrocautery and not a scalpel. The incision must always be distally and proximally extended to one cm of healthy, unburned skin when possible.

Depth of the incisions should be into the subcutaneous fat to allow for sufficient widening of the incision gap. Running a finger along the incision can detect residual restricting areas.

Although only minor bleeding will occur, hemostasis is necessary. Some deep vessels require cauterization or ligation to prevent late re-bleeding, e.g., during patient transport.

It is important to recognize that an escharotomy is not a fasciotomy; when no signs of a compartment syndrome are present, the muscle fascia does not need to be released.

Escharotomy of the neck, although not recommended by everybody, is always performed only along the ventral side, from the base of the skull bilaterally along the ventral margins of the sternocleidomastoid muscles and extending to the clavicles. (figure 1) Sometimes, a suprasternal cross-incision is performed to allow the neck to be in a straight position for intubation. Care must be taken not to damage the superficially situated external jugular veins and the accessory nerve, running from ventral to dorsal half way over the sternocleidomastoid muscle. Damaging this nerve can cause a paresis of the trapezoid muscle.

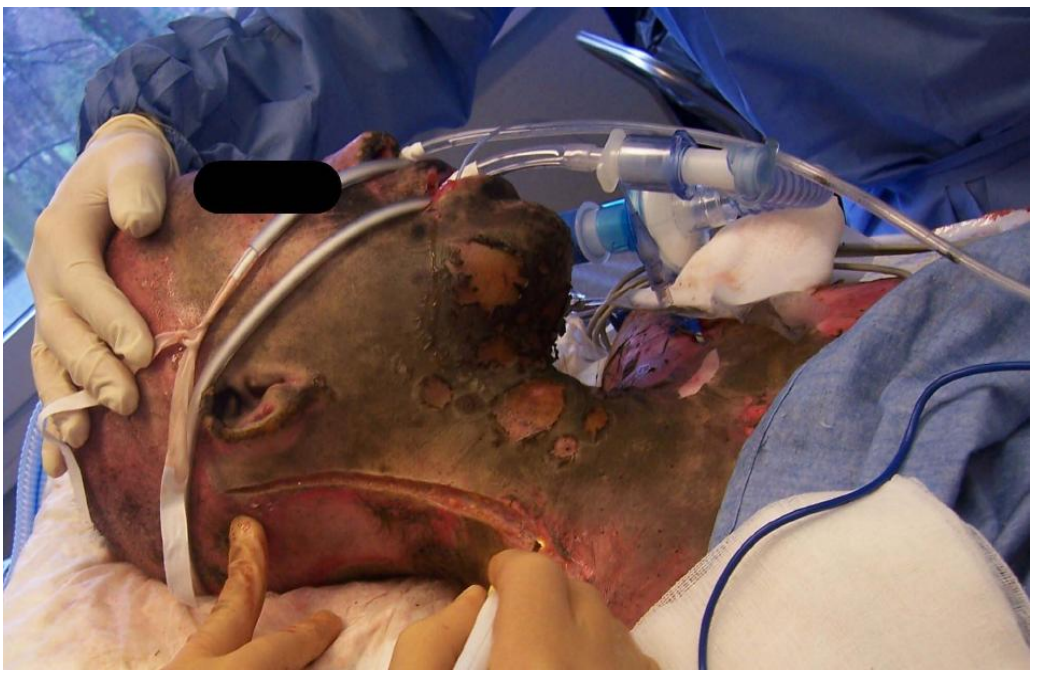

Figure 1. Escharotomy of the neck.

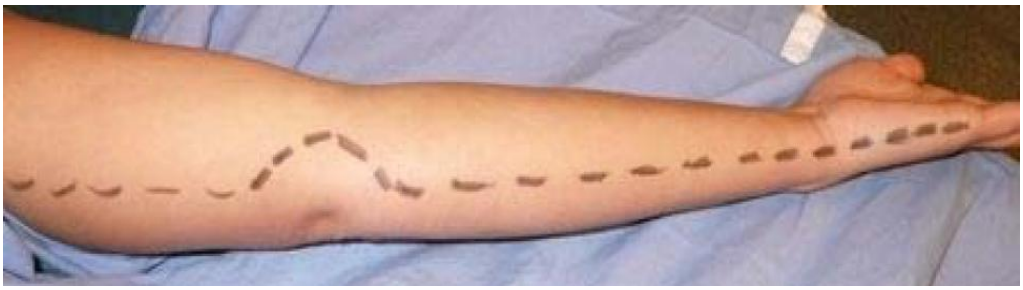

Figure 2a. Drawing of the escharotomy incision line on the ulnarl side of the left arm.

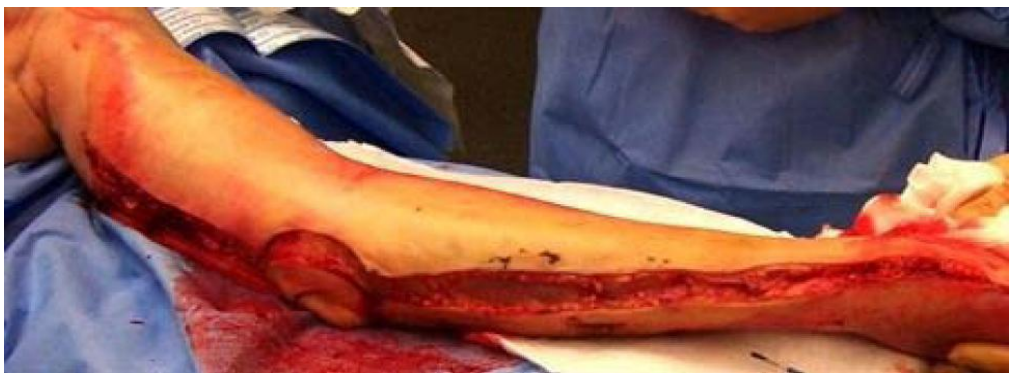

Figure 2b. Escharotomy on the ulnar side of the left arm.

The two incision lines utilized in *the upper extremity* are, from an anatomical position, over the lateral and medial upper arm, cross the elbow joint over the anterior aspect of the medial humeral condyle (taking care not to damage the ulnar nerve), and along the ulnar and radial aspects of the lower arm until the base of the 5 th finger and the thumb. (figure 2a,b)There has been, until now, no clear indication for an escharotomy of the individual digits. Although Salisbury et al. has shown less necrotic phalanges after escharotomy, functional outcomes were not measured. [15] No other evidence for digital escharotomy was found.

Lower extremity incision lines are also run medial and lateral along the upper leg, traverse the knee joint anterior to the fibular head, (thus sparing the peroneal nerve), and down to the ankle joint, taking great care around the dorsal tibial neurovascular bundle and the great saphenous vein just anterior of the medial malleolus. The incisions then continue along the medial and lateral sides of the foot to the base of the first and the 5 th toes (figure 3a,b,c)

In a *truncal escharotomy*, the incision runs in the anterior axillary line from the clavicle (or extended to the neck region) to the lower costal margin, with the incisions connected by a cross incision just below the level of the clavicle and inferiorly beneath the level of the costal margin along the upper abdomen.(figure 4)

Escharotomy of the *abdominal wall* for full thickness burns and intra abdominal hypertension can be performed with the following two perpendicular lines: longitudinal along the axillary lines and in a square fashion in the upper abdomen. (figure 5)

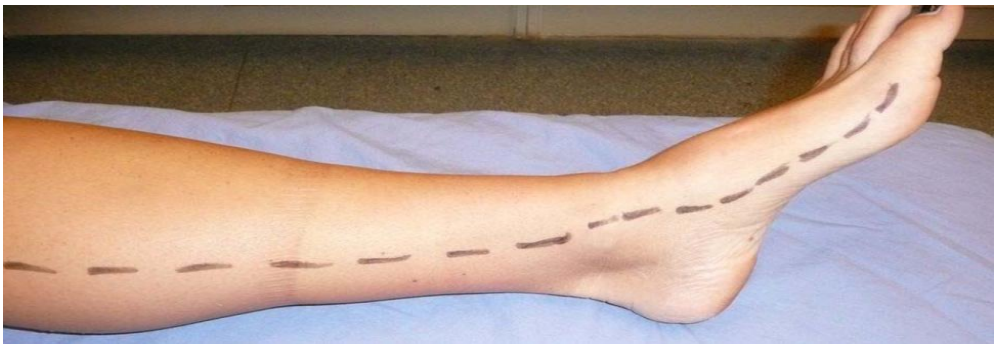

Figure 3a. Drawing of the escharotomy incision line on the medial side of the lower leg.

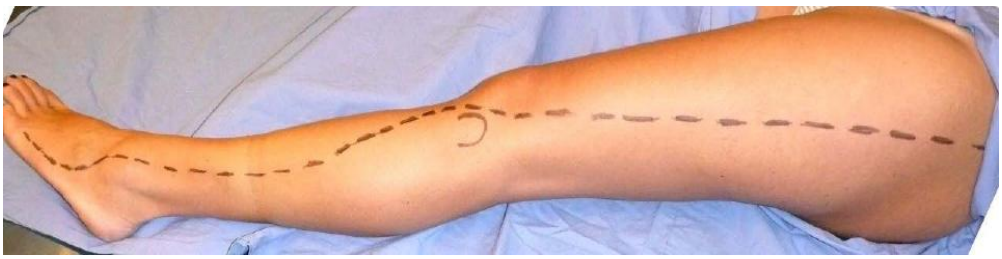

Figure 3b. Drawing of the escharotomy incision line on the lateral side of the leg.

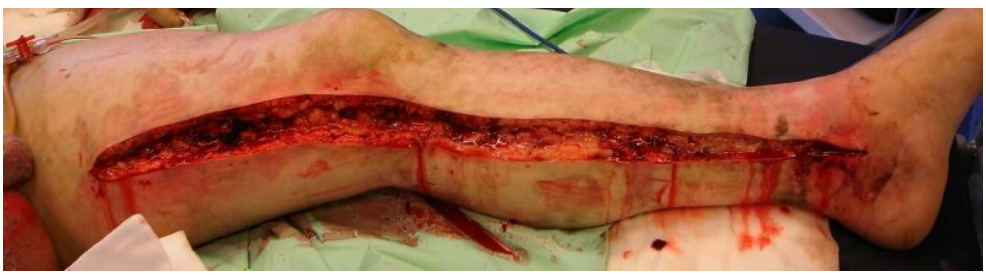

Figure 3c. Escharotomy on the medial side of the left leg.

Some authors recommend an enzymatic escharotomy, performed by enzymatic lysis of the burned skin, but until now there is still not enough evidence to support this procedure. [16]

POST-ESCHAROTOMY TREATMENT

The most important consideration after escharotomy is monitoring of the surgical results, by observing an improvement in perfusion and ventilation or by measuring a decrease in intra- abdominal pressure.

Wound care can be performed by covering the escharotomy incisions with silversulfa diazine and gauze, followed by regular wound inspections.

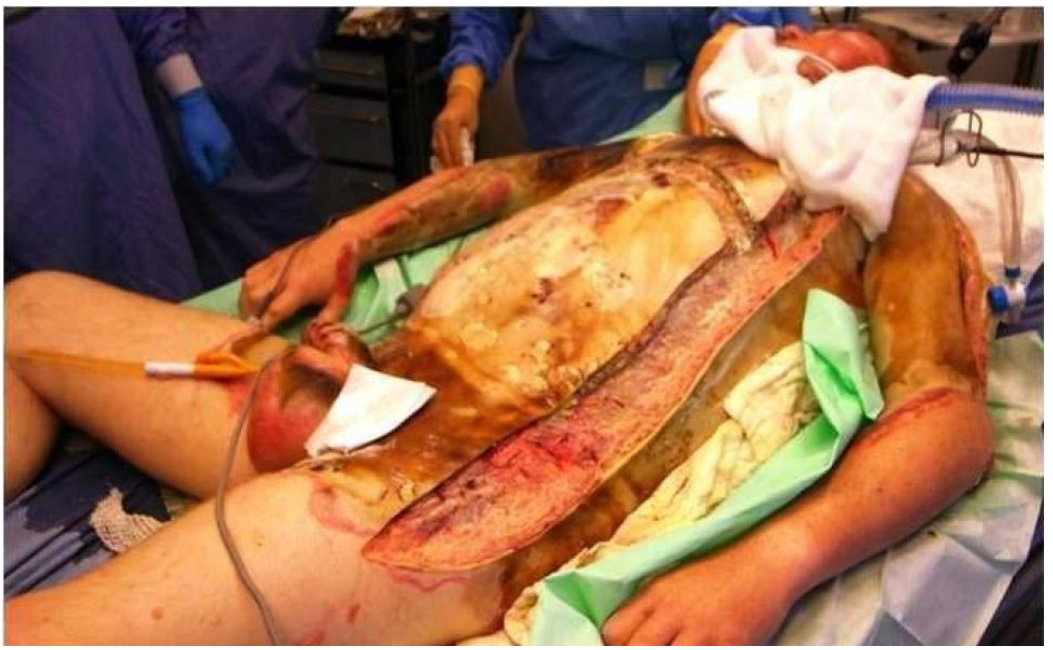

Figure 4. Escharotomy on the left side of the trunk showing the result after relief of the tension.

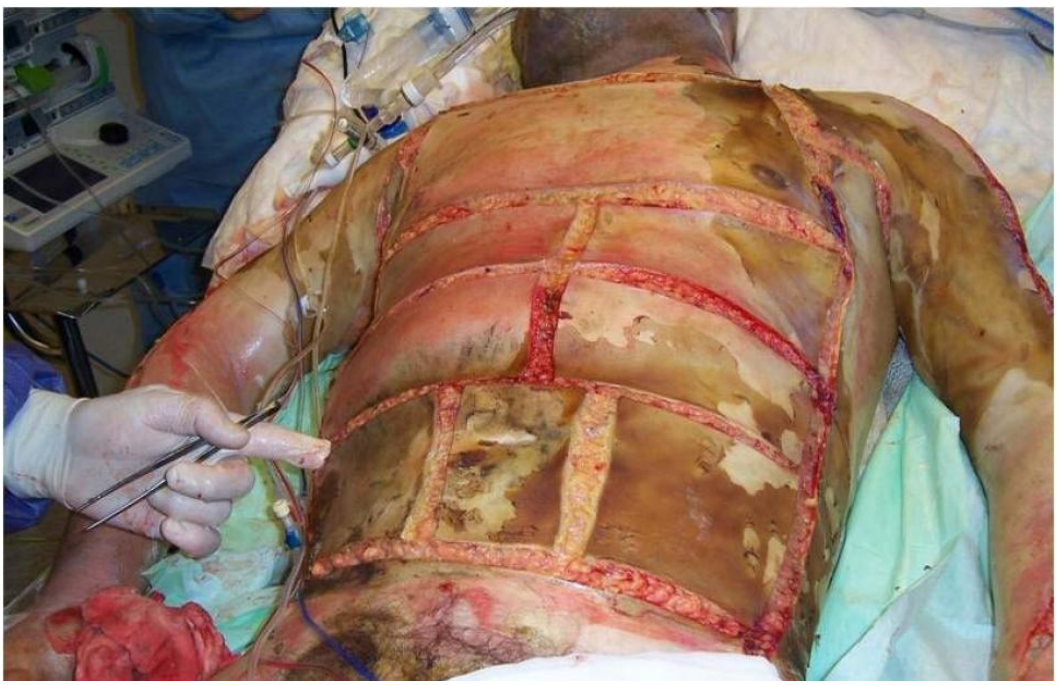

Figure 5. Multiple escharotomies on the thoracic and abdominal wal.

One must also realize that escharotomy is part of a decompression process; other compression syndromes can include compartment syndrome of the extremity (especially in cases of an electric burn) and abdominal compartment syndrome. However, abdominal

hypertension left untreated can lead to abdominal compartment syndrome and can be affected by an abdominal wall escharotomy. This condition will almost always develop at a later period compared to the time frame within an escharotomy has to be performed. However, an escharotomy must be emergently performed as a damage control procedure in severe burns.

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Chapter 13

IMPACT OF BURNS ON THE HEALTH-RELATED QUALITY OF LIFE OF BURNED PATIENTS IN THE REHABILITATION PHASE: INTEGRATIVE REVIEW

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ABSTRACT

Burns are important causes of emergency care for children and adults around the world. Most burn accidents occur at home and male persons are the most affected victims. The main cause of burns in children are hot fluids and, in adults, fire. A burn is a skin tissue injury and can be classified, according to the agent, as physical, chemical, electric and radiant and, according to the injury characteristics, considering the depth (superficial, partial thickness and full thickness burn) and extent of the burned body surface. The following factors influence burn prognoses: depth and extent of the injury; causal agent; contact time between skin and causal agent; age, injury by inhalation and airway burns; preexisting diseases; associated traumas and infection. Like for the burn prognosis, some factors influence burn victims' rehabilitation process and can be directly related to quality of life. It is known that adaptation after the burn implies a long process, influenced by changes in body structure and functioning, body image, emotional condition and socioeconomic and cultural context the person is inserted in. This chapter presents the result of an integrative literature review on impact of burns on the health-related quality of life of burned patients in the rehabilitation phase. Four independent reviewers used six electronic databases (LILACS, PubMed, PsycINFO, CINAHL, Scopus and ISI Web of Science) for the search, based on previously defined inclusion and exclusion criteria. The analysis of 32 studies revealed that burns patients' health-related quality of life is associated with physical, emotional and social aspects. In general, the studies showed that greater trauma severity, inadequate coping mechanisms, dissatisfaction with one's body image, difficulties to establish interpersonal relations and the presence of posttrauma distress are associated with a worse health-related quality of life. Return to work and longer time after the trauma are predictors of a better health-

related quality of life. In the rehabilitation process, victims' individual and social aspects should be taken into account, aiming for their reinsertion in society with as little influence as possible from the trauma and with a better quality of life.

INTRODUCTION

Around one million burns occur per year in the United States; about 500 thousand are attended at emergency services and 40 thousand are hospitalized. Deaths due to burns are the fifth most common cause of non-intentional trauma and the third cause of fatal trauma at home [1]; incidence levels of burns have decreased in recent years though, from ten cases per 1000 in the 1950's to 4.2 per 1000 in the 1990's [2].

In Brazil, unfortunately, there are no precise statistical data on the occurrence of these accidents, but the Brazilian Burns Society estimates a million of burns cases every year, 200 thousand of which are attended at emergency services, while 40 thousand demand hospitalization. Besides, burns figure among the main registered causes of death, behind traffic accidents and homicides [3].

In Brazil, burns are the third cause of emergency care in children, behind falls and transportation accidents. Falls and burns are the most prevalent causal agents in childhood [4]. A downward trend is found as age advances, but traffic accidents and other accident types tend to increase [5]. Thus, burns in childhood represent an important cause of hospital care and hospitalization and lead to relevant physical and emotional sequelae [6]. Most burn accidents occur in the home environment, followed by occupational accidents, and men are the most affected people [7-8]. In other countries, self-extermination attempts [9] and large fires [10] are also frequent causes of burns among adults.

In general, like in adults, burns incidence levels are higher among male children [4-6,11,-12] and among children under five years of age [5,11-13], which may be related with the two genders' different behaviors and with cultural factors, determining boys' more daring behavior, who widely explore the environment they are inserted in and develop more risky activities, making them more predisposed to accidents, as opposed to greater surveillance among girls [6,12,14-15].

Childhood accident events are related to gender, age range, development phase, personality and organic and anatomic particularities, such as physical and/or mental impairment [16]. Most cases among adults are related to occupational accidents for men and domestic ones for women [17].

For children as well as adults, the place where most burns occur is at home [5,11-12,14-15]. Children spend most of their time in the home environment, where they are exposed to the main causal agents of burns, like the handling of hot fluids, chemical and inflammable products, hot metals, stoves, handling of pans, pan handles turned outward, plugs and electrical wires [11-13,18].

In the age range from zero to four years, hot fluids are the main burns causes. Children's psychomotor development, associated with the curiosity to explore the space around them, probably approximates them to places like the kitchen, where there are foods, drinks, oil and other hot fluids which, when spilled on the children, mainly affect the head, neck, upper and lower limbs and trunk [12]. Between five and 14 years of age, on the other hand, flames are more frequent as, at this age, accidents involving the use of ethanol and other inflammable

agents are common. Burns provoked by inflammable agents are deeper, due to the time the skin is exposed to the heat. In Brazil, ethanol is frequently stored in low places at the children's reach, who often get burned due to the lack of adult surveillance and supervision [12].

In many cases, burns result from domestic violence or caregivers' neglect, mainly when they affect children [19-20]. They are also associated with low income and, consequently, with precarious housing, health, education and information access conditions [7,19,21].

Burns can affect the structures, function and appearance of body parts, due to the presence of hypertrophic scars and contractures. It is considered a severe trauma that causes physical, emotional and social sequelae. Esthetic problems after a burn are common among severely burned patients.

Between 1960 and 1980, burns treatment emphasized the acute care phase, including antibiotics therapy, biological dressings and inhalation injuries, with a view to trying to bring down mortality rates. After overcoming this challenge, as from the 1990's, clinical practice and research also started to focus on the rehabilitation of burns victims, in order to help them to return to society [22], with quality of life.

If, on the one hand, advances in burns care play an important role in the decrease of mortality rates among severely burned patients [23], on the other, they have not been effective in the rehabilitation of victims who survive with severe sequelae. Thus, knowledge on the clinical and psychological therapeutics of burns patients has increased each decade, through new technologies, drugs, dressings and specific surgeries, so that a considerable number of survivors face a long rehabilitation period [2].

Recovery after severe burns takes long, and some people can continue experiencing symptoms deriving from this trauma for years [24-25]. The rehabilitation process of burns victims involves overcoming psychological, physical and social damage, directly related with the quality of life of victims and their families, including the denial of bodily changes; problems regarding physical activities due to tissue retractions, pain and scar treatment; and difficulties to return to work, school and social contact [26]. Besides, manifestations of posttrauma stress [27-28], distress [29-30], psychological vulnerability, anxiety [31], dissatisfaction with one's body image [32], depression [33] and feelings of threat [29] have been associated with post-burn trauma, also impairing victims' quality of life [34].

It is important to find out about the nature of patients' psychological response towards the burns, at different times [35]. Researchers have demonstrated that a significant number of patients have displayed high levels of anxiety, depression and despair in the initial rehabilitation phase [35-36]. Each person reacts in one way, depending on environmental and constitutional factors [37-38], which is why the identification of patients' individual coping standards can be of help in short and long-term adaptation after the burn, positively collaborating with rehabilitation [35]. It is therefore important to improve knowledge on the factors interfering in these people's psychosocial rehabilitation, with a view to improving care planning and assistance to this clientele. Instruments to assess this care are also needed.

Assessing the quality of life of people who survived severe burns is necessary to get to know the true impact of this trauma, and also to be able to assess the results of interventions and treatment advances. Quality of life assessment has become increasingly present in health, probably due to the enhanced life expectancy and survival of people with chronic conditions [39].

A study has demonstrated that burns victims consider that the modifications deriving from the trauma entail a loss of quality of life, due to different factors, such as the time spent to take care of the burns; difficulty to return to normality; physical limitations; impaired family relations, mainly in affective and sexual relations with partners; decreased autonomy to accomplish simple and daily activities and work-related difficulties [39].

There is no universal consensus on the quality of life concept [30] and various authors have considered its measurement difficult [40-41]. The World Health Organization offers a broad definition of quality of life, which can be understood as "individuals' perception of their positions in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" [42]. Quality of life can be understood as a multidimensional and multifactorial mosaic [43]. In addition, the concept of quality of life quality of life is often misunderstood, for example, in relation to perceived health status and health-related quality of life (HRQoL). The health status perceived by the patient is related to the physical condition that reflects the individual's punctual (momentary) status and HRQoL in terms of the health status, functional capacity, duration of life, consequences of symptoms or injuries deriving from the illness, treatment or opportunity for health [44].

In view of recent progresses in burns treatment and rehabilitation; the need to help burns patients and their families to adapt to the changes deriving from the trauma; and the difficulties found in literature regarding the quality of life concept, research is needed to summarize knowledge on the impact of burns on the health-related quality of life of burns victims. Thus this integrative literature review aimed to describe the impact of burns on the health-related quality of life of burns victims during the rehabilitation phase.

METHOD

Due to the quantity and complexity of information in health, integrative literature reviews are fundamental resources. This method aims to join and summarize research results on a certain theme or question, in a systematic and ordered theme, contributing to expand knowledge on the research theme [45]. The initial goal of this research method is to obtain an in-depth understanding on a certain phenomenon, based on earlier studies [46]. For the reader to identify the true characteristics of the studies included in the review, it is fundamental to follow methodological strictness and clarity in the contents of results [47].

Procedures

To develop this integrative review, the six phases Whittemore & Knalf (2005) proposed were followed: 1. Definition of the guiding question; 2. search and selection of papers; 3. extraction of papers included in the integrative review; 4. assessment of studies included in the integrative review; 5. interpretation of results and 6. presentation of the integrative review [48].

The question that guided this review is "What is the impact of the burn on the health-related quality of life of burns patients in the rehabilitation phase?"

To search the papers, four reviewers independently used six electronic databases (Latin American and Caribbean Health Sciences Literature-LILACS, PubMed, PsycINFO, CINAHL, SCOPUS and ISI Web of Science). The criteria to include articles in the review were: 1. Studies aimed at assessing the HRQoL of burns patients; 2. Studies published between 1999 and 2010; 3. Studies in English, Portuguese and Spanish. In the search strategy, the following health descriptors were used, with different combinations: quality of life, health status, questionnaire and burns; and the key words: tools, scale and assessment.

After crossing the databases, 1038 papers were found. When selecting the papers, four reviewers read each abstract and confirmed its inclusion or not. In case of disagreement, the reviewers discussed each situation until reaching a consensus. The final sample resulted in 32 papers. Twenty-five of these came from PubMed, four from SCOPUS, two from CINAHL, one from the Web of Science. In LILACS, none of the papers complied with the inclusion criteria; and, in PsycINFO, only one paper was selected, which had already included by PubMed though (Picture 1).

To collect and register the data extracted from the papers, an instrument adapted from Ursi (2005) was used, which was modified and submitted to face and content validation [49].

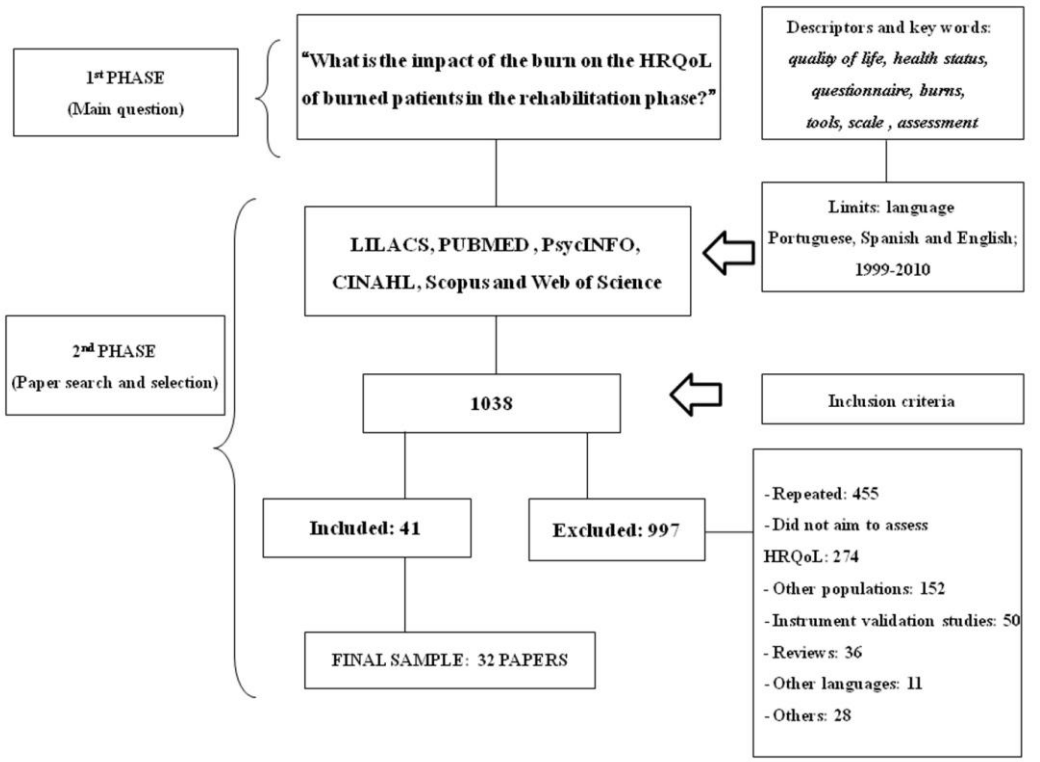

Figure 1. Flow chart of the integrative review phases.

RESULTS AND DISCUSSION

The full versions of 32 papers were analyzed. All studies are quantitative, with a non-experimental design. Twenty-four were cross-sectional and eight longitudinal (Table 1).

Table 1. Description of the studies selected for the review

Authors	Sample	Method: Instruments used
LONGITUDINAL STUDIES		
Corry et al. (2010) [50]	(n) initial: ND* (n) final: 171	Short Form of the McGill Pain Questionnaire (MPQ-SF); Davidson Trauma Scale (DTS); SF-36 Health Survey (SF-36)
Dodd et. al. (2010) [51]	(n) initial: 181 (n) final: 145	Questionnaire with demographic data and Burn Outcome Questionnaire (BOQ)
Pavoni et al. (2010) [52]	(n) initial: 50 (n) final: 19	European Quality of Life 5-Dimension (EQ-5D)
Fauerbach et al. (2005) [53]	(n) initial: ND* (n) final:162	Brief Symptom Inventory (BSI); Global Severity Index (GSI); SF-36
Williams et al. (2003) [54]	(n) initial: 304 (n) final: 216	Sickness Impact Profile (SIP)
Cromes et al. (2002) [30]	(n) initial: 110 (n) final: 69	Burns Specific Health Scale; BSI; Functional Assessment Screening Questionnaire (FASQ); Functional Independence Measure (FIM); Pain Analog Scale (PAS); Community Integration Questionnaire (CIQ) and Satisfaction with Life Scale (SLS)
Fauerbach et al. (2000) [32]	(n) initial: 86 (n) final: 86	Satisfaction with Appearance Scale (SWAP); DTS; Beck Depression Inventory (BDI); SF- 36
Fauerbach et al. (1999) [55]	(n) initial: ND* (n) final: 86	DTS; BDI; SWAP; Life Orientation Test (LOT); SF-36
CROSS-SECTIONAL STUDIES		
Salvador-Sanz et. al. (2010)[56]	(n) initial: 367 (n) final: 115	BSHS; Questionnaire with clinical and socio-demographic data
Landolt et al (2009) [27]	(n) initial: 60 (n) final: 43	Clinician-Administered PTSD Scale for Children and Adolescents (CAPS-CA); TNO-AZL Child Quality of Life Questionnaire (TACQOL)
Novelli et al. (2009) [57]	(n) initial: 42 (n) final: 30	SIP
Sanchez et al. (2008) [58]	(n) initial: 898 (n) final: 813	EQ-5D
Baker et al. (2007) [59]	(n) initial: 83 (n) final: 83	Young Adult Self-Report (YASR); Structures Clinical Interview for Diagnosis (SCID); SF-36; Quality of Life Questionnaire (QLQ)
Dyster-Aas et al. (2007) [28]	(n) initial: 128 (n) final: 86	Swedish universities Scales of Personality (SSP); BSHS-B; Tampa Scale of Kineisiophobia (TSK); Impact of Event Scale-Revised (IES-R)
Pope et al. (2007) [60]	(n) initial: 77 (n) final: 77	Body Esteem Scale for Adolescents and Adults (BES); SWAP; BDI; Youth Quality of Life Instrument (YQOL)
Lebleci et al. (2006) [61]	(n) initial: 22 (n) final: 22	SF- 36
Moi et al. (2006) [62]	(n) initial: 143 (n) final: 95	SF-36; Quality of Life Scale (QOLS)
Noble et. al. (2006) [29]	(n) initial: 22 (n) final: 22	BSHS-B; Coping with Burns Questionnaire (CBQ) e Pain Patient Profile (P3)
Rosenberg et al. (2006) [63]	(n) initial: ND* (n) final: 95	Quality of Life Questionnaire (QLQ)
Willebrand et al. (2006) [64]	(n) initial: 86 (n) final: 86	Tampa Scale of Kinesiophobia (TSK); BSHS-B; SSP
Anzarut et. al (2005) [65]	(n) initial: 189 (n) final: 47	BSHS-Abbreviated (BSHS-A) and SF-36

Authors	Sample	Method: Instruments used
CROSS-SECTIONAL STUDIES		
Druery et. al. (2005) [23]	(n) initial: 38 (n) final: 25	BSHS-A, an additional questionnaire with specific questions on physiotherapy and occupational therapy
Kildal et al. (2005) [66]	(n) initial: 161 (n) final: 161	CBQ; BSHS-B
Willebrand et. al. (2005) [67]	(n) initial: 116 (n) final: 84	SSP; Hospital Anxiety and Depression Scale (HADS); IES-R; BSHS R
Cochran et al. (2004) [43]	(n) initial: 76 (n) final: 32	SF-36
Dyster-Aas et al. (2004) [68]	(n) initial: 97 (n) final: 86	BSHS-B
Kidal et al. (2004) [69]	(n) initial: 350 (n) final: 166	SSP; BSHS-B
Pallua et al. (2003) [33]	(n) initial: 153 (n) final: 92	ALLTAGSLEBEN; Center for Epidemiological Studies Depression (CES-D); General Health Questionnaire (GHQ); Ways of Coping-Checklist; Hannover-Transplantation-Rating-Scale
Altier et al. (2002) [70]	(n) initial: 121 (n) final: 49	Symptom Check list 90 Revised (SCL-90R); GSI; SF- 36
Kildal et al. (2002) [71]	(n) initial: 181 (n) final: 145	BSHS-A; BSHS-Revised) and BSHS-B
Landolt et al. (2002) [72]	(n) initial: 133 (n) final: 105	Child Behavior Checklist (CBCL); TACQOL; Family relationship index (FRI)
Sheridan et al (2000) [73]	(n) initial: 80 (n) final: 68	SF-36

* ND- not described.

The collected data were grouped in three categories, described below: “The severity and impact of the burn”; “Personality, coping strategies and impact of the burn”; “Emotional and social impact of the burn” and “Impact of the burn on the health-related quality of life during the rehabilitation process”.

THE SEVERITY AND IMPACT OF THE BURN

One of the most important factors that can affect the quality of life of a burn victim is trauma severity. In general, burns that require admission to a Burns Unit are severe to a certain extent. A set of variables is used to estimate the burn severity. The main are the total body surface area (TBSA) percentage, duration of hospital stay, posttrauma time, number of surgeries, simultaneous face, hand and genital burns, need for grafts and gender [56]. Various studies have shown the relation between one or more of these aspects and worse adaptation [28,33,56-58,65]. The depth and extent of a burn are related with the type of agent, which is another variable that can contribute to trauma severity.

A study of Spanish burned patients showed that burn severity, assessed by larger TBSA percentage and longer hospital stay, affects HRQoL, which decreased according to the increase in burn severity [58]. In another study, also involving Spanish patients, it was observed that posttrauma time, number of surgeries and TBSA percentage predicted a worse quality of life, mainly influencing the affect, body image and interpersonal relations domains of the Burns Specific Health Scale – Brief [56]. Pavoni et al. (2010) assessed mortality and quality of life among burns patients. Out of 50 study participants, 22 died, mainly due to infection [52]. The results showed that both the physical and psychological consequences of

the burn influenced quality of life and that, one year after the trauma, the study participants who suffered severe burns still reported impaired functional skills, like in mobility and activities of daily living for example [52].

Another study showed that full-thickness burns and hand function impairments predicted worse HRQoL results when considering the physical domain of the SF-36. In the same study, however, larger TBSA, gender, body area affected by the burn, need for tracheotomy and days on mechanical ventilation did not predict a worse quality of life [65].

Dodd et al. (2010) assessed the impact of hand burns on the quality of life of children at three, six, 12, 18 and 24 months posttrauma [51]. The authors compared children between zero and 18 years of age, with and without hand burns, and concluded that hand burns associated with high TBSA percentages indicate trauma severity and predict the need for further resources and that maintaining the functioning of hands and feet is important for quality of life [51].

The injury location can be an important contributing factor to increase trauma severity, not only due to its visibility and consequences for the victim's appearance, but also due to the sequelae and degree of limitation it can cause. Joint burns are considered severe because they can lead to joint contracture, reducing the victim's movement range. In a HRQoL assessment of patients with joint contractures, using the SF 36, the authors found that the group whose joints were affected by the contracture showed significantly lower scores in the Physical Functioning, Physical Role, Bodily Pain and Vitality domains, which may represent a great functional limitation [61]. Hand and face burns can hamper the reintegration of burns victims, as Pallua et al. (2003) showed [33]. Another study found that, more than two years posttrauma, burned patients between 13 and 72 years of age did not present difficulties to restart functional and self-care activities, especially when the hands had not been affected [23]. Thus, besides joint contractures, hand and foot burns can be a great problem, considerably limiting victims' activity accomplishment and reintegration.

Another important variable is gender. In general, women are more sensitive to appearance changes, which may influence the way they face rehabilitation and adapt to the new condition. Novelli et al (2009) showed that burns affected women more than men [57]. Similar results were found by Kildal et al. (2002) [71].

Burn depth was also associated with a worse HRQoL in a study that assessed burned patients, applying three versions of the Burns Specific Health Scale (Abbreviated, Revised and Brief) [71]. Burns produced by electrical agents tend to go deeper than those produced by thermal agents, which has motivated some studies on the impact of burns provoked by electrical agents on quality of life [29,43]. The result of a study that compared HRQoL assessed by the SF36 and the frequency of return to full-time work among victims of burns by thermal and electrical agents did not show any significant difference [43].

PERSONALITY, COPING STRATEGIES AND BURN IMPACT

Some behaviors and personal characteristics, related with personality traits, as well as coping strategies, may be associated with decreased HRQoL after the trauma. Fear-avoidance behaviors are psychological manifestations associated with traumas and conditions that cause pain, generally related with movement. In burns victims, it was observed that, participants

with a moderate or high level of fear-avoidance were more likely to describe their health as poor and had a longer sick leave than those with a low level of fear-avoidance [64]. This manifestation is associated with physical and emotional aspects and work. Avoidance was a coping strategy also associated with marital status and housing conditions [66], while neuroticism was associated with psychosocial health problems and personality traits [64]. Another study identified that neuroticism is related with health perception over time after the burn event and that its effects are not restricted to the psychosocial aspects of life, but also involve physical aspects [69].

Research has shown the relation between greater functional impairment and worse coping. When greater functional impairment is related with the burn, social avoidance, depression and complaints increase. Social avoidance has been associated with visibility and greater TBSA, accompanied by a decrease in the number of friends and social activities [33,57]. It is observed that an increase in physical function impairments and burn visibility leads to social isolation and to difficulties to close and maintain friendships. On the opposite, domestic activities like watching television and reading increase [33,74].

Another study assessed the psychological functioning and HRQoL of severely burned patients, comparing the results of these people with those of healthy students. The results showed that severely burned patients adapted relatively well and that approximately 25% of patients displayed psychological disorders, in comparison with 12% in the control group. In general, the quality of life of burned patients was good, like in the control group, although they presented greater deterioration in the general health status [70]. There are various possible explanations for this situation, such as greater ability to accept limitations for example, a consequence of overcoming the suffering experienced during hospitalization, as well as the development of coping mechanisms. These aspects demand further study. One example is the relation between social desirability and the health status. A study on the relation between social desirability, assessed through the Swedish University Personality Scale, and the health status, assessed using the Burns Specific Health Scale, showed that individuals with high social desirability levels presented a worse perceived health status in the sensitivity to heat, work and body image domains when compared to people with normal social desirability levels [67].

EMOTIONAL AND SOCIAL IMPACT OF THE BURN

Return to work is an important sign of rehabilitation results, frequently associated with good adaptation. Less severe burns in terms of extent and depth, and patients' positive coping strategies contribute to a better rehabilitation and return to work [28]. In addition, not working after the trauma can be associated with a worse HRQoL [28].

Dyster-Aas et al. (2004) identified that patients who were victims of occupational accidents and were not working after the burn reported a worse health status in the affect, body image and interpersonal relationship domains of the Burns Specific Health Scale Brief and displayed low scores for therapeutic regimen, besides reporting greater pain problems than patients who were working [68].

A study on electrical burn victims' difficulties to return to work showed that, among patients who returned to work, few performed the same tasks as before the burn and that

burns caused by high tension and higher TBSA percentage are associated with worse quality of life scores [29].

Some studies have reported that, after a burn, negative changes occurred in life, mainly influenced by the functional impairment the burn causes [33], which hampered the accomplished of housework activities [57].

A longitudinal research that assessed patients at two months after hospital discharge and six and 12 months posttrauma showed that return to social, housework and work activities occurred six and 12 months after the burn [30].

In a study on the impact of body image on the HRQoL of burned patients, Fauerbach et al. (2000) showed that dissatisfaction with body image is related with prolonged HRQoL difficulties in the Physical functioning and Mental health domains. Patients who showed greater dissatisfaction with their body image, assessed using the Satisfaction with Appearance Scale, presented more extensive burns, more frequently affecting the face, more severe depression and posttrauma stress [32]. Dissatisfaction with one's body image, burn severity, and negative affect influence adaptation, according to the mental health domain of the SF-36. These study results suggest that interventions are important, involving individuals who display dissatisfaction with their body image, as well as preventive interventions for patients at greater risk of dissatisfaction with their body image, such as high TBSA percentages and facial burns [32].

A study that compared 36 British young people who had been burn victims in childhood (at an average 11 years posttrauma on the interview date) with 41 young students without burns found that burn survivors displayed a significantly more positive assessment of how other people perceived their appearance, as well as greater satisfaction with their weight and a better quality of life [60]. According to the authors, burn survivors may develop coping mechanisms that enable them to go beyond appearance, possibly making them stronger than young students without burns [60]. The importance granted to appearance is related with the cultural context people live in. In Brazil, strong concern with one's bodily appearance exists, which is frequently exposed due to the hot climate [75].

Another study examined the quality of life of pediatric burn survivors at the transition from adolescence to adult age. The results were compared with those of the normal population and showed that young adults obtained lower total quality of life scores [63].

Fauerbach et al. (1999) investigated the influence of postttrauma distress on HRQoL after a severe burn [55]. Based on the American Psychiatric Association (1994), the authors consider posttrauma distress as moderate symptoms of post-traumatic stress disorder, characterized by symptoms related to intrusive thoughts, which refer to repeated thoughts on the burn experience, avoidance and persistent symptoms related to sleeping difficulties, chronic anxiety and hyperarousal [76]. They concluded that posttrauma distress is related with impairments in the physical and psychological adaptation of severe burn survivors, based on pretrauma adaptation levels. Posttraumatic stress disorder was also appointed as a predictor of worse physical and social functionality and greater physical and psychosocial disability to years after hospital discharge; its effect on physical functionality decreases over time though. Between six and 24 months posttrauma, high posttraumatic stress scores were related with worse social, physical, psychosocial functionality and vitality [50].

IMPACT OF THE BURN ON HEALTH RELATED QUALITY OF LIFE ALONG THE REHABILITATION PROCESS

Time has been an important variable to define a better quality of life, return to activities of daily living and return to work for burn victims. In this respect, studies have shown that, for one year after the burn, physical and psychosocial functions and health status improve, but remain stable after that period [54,73].

Time since injury is also considered a predictor of better emotional and physical performance in children and adolescents under multiprofessional follow-up for two years [73]. Due to the slow recovery of a severe burn victim, it is often considered that this person cannot be decisively discharged. Childhood or adolescence burns may demand a lot of time and several surgeries before definitive discharge. This situation may arouse unreal expectations about the reparatory surgery results and the feeling that the result is never permanent. Nevertheless, some longitudinal studies have shown that, as physical symptoms improve, as early as in the first six months, a better HRQoL is observed [30,59].

Sheridan et al. (2000) observed that, four months after the burn, children who had returned to the activities they accomplished before the accident displayed better general health, physical functionality and functional performance scores [73]. The same study also showed the importance of social support, as children affiliated with better functioning families revealed higher scores in the Physical Role domain of the SF36. Landolt, Buehlmann, Magg and Schiestl (2009) assessed child burn survivors who had experienced at least one graft due to the injury depth and found evidence of high posttraumatic stress prevalence levels in child burn survivors and its negative association with health related quality of life [27]. These results appoint the need for identification and immediate treatment of burned children with posttraumatic stress, with a view to minimizing psychological morbidities and improving their quality of life. On the other hand, a good family relationship standard and the occurrence of burns in young children were the only significant predictors of a good quality of life in the study by Landolt, Grubenmann and Meuli (2002), who interviewed parents of child burn survivors [72]. Those study results indicate that families with interaction difficulties among their members and whose burned children are at a more advanced age should be closely monitored, including psychological support.

In adults, it was demonstrated that, more than five years after the accident, physical aspects improve, such as simple skills, hand function, heat sensitivity, body image, satisfaction with work and with the therapeutic regimen [29]. Other aspects, such as affectivity, sexuality and interpersonal relations, showed little change along five years after the burn [29].

At one month after hospital discharge, it was observed that patients experienced difficulties for leisure, taking care of the house, sleeping, relaxing, as well as impaired emotional behavior [54]. In another study, it was observed that, within one year, the areas the burn most affected were work, emotional behavior, housework administration, leisure, rest and social interaction, with improvements occurring after that time. Many had not returned to work during that period and displayed psychological and sleep problems [57]. Emotional aspects like the presence of pain and distress were associated with a worse quality of life, mainly at two months after hospital discharge [30]. Less emotional problems before the burn and younger ages were variables associated with less influence on emotional aspects at two

years after hospital discharge and pain was related with worse functionality at six and 24 months after hospital discharge [50].

Pain is directly related with anxiety. A vicious circle is established, in which main exacerbates anxiety, which exacerbates the pain [77]. In a study of young adults (between 18 and 28 years of age) who had been victims of burns in childhood or adolescence found that most victims were capable of accomplishing self-care activities that required mobility; they did show higher anxiety levels and a lower HRQoL (assessed through the Quality of Life Questionnaire) in comparison with the normal population. Although no relation was found between lower HRQoL and physical problems, this indicated that little attention has been paid to this group during the rehabilitation phase [59].

The result of a study involving burned patients in Norway showed that, despite their worse health status, they indicated a good quality of life, with results similar to the general population. These patients showed low scores in the Physical Function, Role Physical, General Health, Social Function and Role Emotional domains of the SF36 [62].

The results of a research that followed a group of 72 burns patients during one year showed a better average health status for burn victims, assessed using the Sickness Impact Profile, during the first and twelfth month posttrauma. The Sickness Impact Profile is divided into three major dimensions: Physical Function, Psychosocial Function, and Independent Categories. The first dimension, Physical Function, includes three categories: 1) Ambulation, 2) Mobility, and 3) Body Care and Movement. The second dimension, Psychosocial Function, includes four categories: 1) Communication, 2) Alertness Behavior, 3) Emotional Behavior, and 4) Social Interaction. The authors recommended that these categories should be not considered independently. In that study, the authors found that the Physical function and Psychosocial function dimensions of the Sickness Impact Profile improved during the first and twelfth month, remaining stable [54].

In a study on the impact of the burn, Fauerbach et al. (2005) found that greater psychological distress during hospitalization is associated with greater physical and psychological impairment, leading to role disruption, even at six and 12 months posttrauma [53].

CONCLUSION

A large number of variables need to be taken into account when assessing the impact of a burn on quality of life. Many of the aspects discussed in this review are related to trauma severity and the victim's reaction, which depends on individual factors, involving personality traits and cultural aspects.

Studies showed that the impact of this trauma affects different aspects of people's lives and, frequently, friends and relatives. In general, research demonstrated that greater trauma severity, inadequate coping mechanisms, dissatisfaction with one's body image, difficulties to establish interpersonal relations and the posttrauma distress diagnosis are associated with a worse HRQoL. Return to work and longer time posttrauma predict a better HRQoL. In this context, efforts should be made to prevent burns, as many accidents could be provided through simple prevention measures.

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Chapter 14

PSYCHIATRIC ASPECTS IN BURN PATIENTS

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ABSTRACT

After an epidemiological analysis of psychiatric disorders as a consequence of burns and also psychiatric aspects of burn victims before the accident, this paper discusses the correlation between psychiatric disorders and burns from the epidemiological, etiopathogenetic and clinical-therapeutic aspects.

Burn patients often suffer from psychiatric disorders and there is a clear connection between the extent and/or severity of injuries (TBSA) and mental illness, particularly anxiety, mood disorders, and post-traumatic stress disorder.

The occurrence of psychiatric disorders (mainly substance or alcohol abuse/dependence, suicidal behaviour, schizophrenia and personality disorders – antisocial or borderline) is a clear-cut risk factor for those with burn injuries.

The occurrence or onset of psychiatric illness during burn hospitalization or recovery is a negative factor for wellbeing and also for the quality of life in the medium-long term.

A burn injury is a traumatic experience for patients, not only as regards psychological aspects (no integration of the traumatic experience with self-perception of life) but also personal ones (knowledge of self-vulnerability, difficulty in accepting the new aspect of the body, with its possible deformation and scars) after trauma. All aspects which may refer to primordial and psychoanalytic fear of death must be taken into consideration. It is also necessary to consider the concepts of accident proneness and consequent pre-burn impulsivity, which may anticipate/represent a person's predisposition to a traumatic event.

All these concepts have clinical and therapeutic importance for multidisciplinary care.

This chapter focuses on the relationship between burn injuries and psychiatric illness: post-traumatic stress disorder (acute and chronic), affective disorders, and personality traits. They must all be examined not only as regards their outcomes but also the patient's pre-trauma psychopathology and susceptibility. Also of importance is facing

therapy for all these disorders and its correlation with burn care (in terms of length of hospital stay, quality of life, and functional and psychological results).

INTRODUCTION

*"*Every scar is an indelible mark, an obstacle to forgetting, a sign that makes of body a memory".
(U. Galimberti)
"We must change to react to what we undergo. Because the problem is not in what we encounter, but in our attitude towards it"
(Akong Rimpoche)

Suffering severe burns (TBSA > 25% and 3rd-degree burns) is a dramatic event for an individual's psychophysical integrity. If we consider as "traumatic" an event which involves an individual's affective, physical and social aspects, to such an extent that person exceeds a certain physical, medical and social threshold, together with the capacity for coping with it in a suitable time-frame (Pavan 1996), then burns are definitely traumatic. The relationship between trauma and the onset of psychological disorders is well-known, studied and documented. Many authors (Janet, Jaspers, Meyer, Seyle, etc.) have contributed to describing Post-Traumatic Stress Disorder (PTSD) and identified the vulnerability of the mind to events which become an unbearable threat to an individual's psycho-physical homeostasis. In these dynamics, we call traumatic not only true external traumas, but also life-events (Paykel) which may, in certain subjects, evoke feelings of vulnerability and eventually induce pain and disorder.

Concepts of Trauma Psychoanalysis

The concept of trauma (from the Greek *τραυμα,* wound) is a central element in psychoanalysis.

At the beginning of his analytic theorization, Freud speculated on trauma as a consequence of real primary events of the child (more or less pertaining to the sexual sphere). Trauma then assumed a less real and more psychical character (the child's experience of anxiety about abandon/death). This experience is often linked to parental figures, shifting the axis of the traumatic event from external trauma to an event subjectively felt as traumatic. It is this first experience, undergone as traumatic and uncontrollable, which emerges with each following traumatic experience. Psychoanalysts after Freud developed various theories to explain the relative importance of external traumas and of the primordial traumatic event in promoting the development of psychopathology after such traumas. A common point is the definition of "traumatic" for everything which cannot be elaborated and eventually made "conflictual", which must then be interpreted and sublimated. Psychopathology may be explained in different ways, i.e., depending on the reaction of a subject to loss/separation from the significant Other, from the "good-enough" mother or "not-good-enough" mother (Winnicott) or on how the subject was able to construct personal narcissism (normal or pathologic). James (1960) stated that trauma may often be considered not as something

exceptional, but as too close to the subject's developmental stage at the moment when it occurs.

Other theories seek to explain the role of trauma in the development of psychopathology in changing dynamics: either in the family (Douglas) or in the fixation of traumatic experiences in the mind of an unprepared subject who is unable to remove them, so that instead of being neutralized they remain bound (Semi, 1989). Some authors state that subsequent micro-traumas can potentially induce pathology as a threat to the integrity of the Self, etc. (due to a lack of self-confidence and primary integrity).

On a phenomenological level, Lacan (1979) believes that the "real of trauma goes beyond the dreams", implying another interesting concept: that the "space" of trauma differs significantly from the analytic space of dreaming, which is evanescent and brief with respect to the reality of the traumatic experience, which tends to re-occur and perpetuate itself with a nearly omnipresent temporal logic. Also, unlike dreaming, the logic of trauma is not caused by something symbolic or interpretative, because a trauma could be represented like an invincible event which threatens the integrity of the subject's personality and body, a body which feels pain and which manifests it with true physical symptoms. Lastly, the truth of dreams is always symbolic, whereas trauma is always unveiled reality.

Whichever theory is preferred, a traumatic experience is something which distorts a person's inner homeostasis, both primitive homeostasis, related to the formation of the Ego and relationships with parental figures, and the secondary, refined homeostasis which a person develops with life and experiences.

An exhaustive description of the various psychoanalytic theories on trauma is not the aim of this work. However, it is clear that a traumatic experience is such with regard to the level of "preparation" of a subject's Ego, and therefore to a condition deriving from relationships with parental figures and primitive traumatic experiences which influenced the formation of that Ego.

It is possibly this way of functioning of the psyche, of the formation of an Ego from the integration of primordial experiences with later secondary experiences, that leads in some cases to a sort of vulnerability and a tendency to relive and repeat trauma. Freud himself observed such a tendency, which led him to postulate the theory of the so-called "death wish". The accepted concept under which this phenomenon is now known as "accident proneness" (see later).

In the approach to patients, it is of the utmost importance to understand the significance of the traumatic experience, whether derived from parental relationships or primordial traumas. We must be able to understand the psychic structure in order to identify the presence or absence (and, in the latter case, the reason for that absence) of the awareness that trauma, as an external event, also involves the inner self and threatens a person's narcissistic homeostasis, which is forced to face limitations; Lastly, we must understand why the subject is led to repeat traumatic experiences based on past experiences.

BURNS AND PSYCHOPATHOLOGY

In the case of burns, there is a rich literature describing close relationships between the development of several psychological disorders and the burn event (in particular at 1 year) [19, 50] (Ilechukwu ST, 2002; Tedstone JE et al, 1997):

- Post-traumatic stress disorder [35,36,37] (PTSD), both acute and chronic, is often related to reduced tolerance to pain [49] (prevalence at 1 year: 13-45%) (Palmu et al, 2010; Palmu et al 2011; Taal and Faber, 1998).
- Major depression [35,36,37], related to the degree of body surface modifications [28] (Madianos et al, 2001), and also occurring in patients who require reconstructive surgery for post-burn sequelae (prevalence 15-65%) (Palmu et al, 2010);
- Major prevalance of drug abuse (prevalence 27.2%) [35,36](Palmu et al, 2010);
- Disorders due to changes in body image [52] (Thombs et al, 2007), more or less associated with depression [53] (Thombs et al, 2008), important in recovering not only the Self image, but also of social life;
- Anxiety disorders [15] (prevalence 15-21%, both acute and chronic) (Franulic et al, 1996);
- Sleep disorders, in particular recurrent nightmares [25, 26] sometimes years after the event (Low et al, 2003; 2006).

Relationships have also been defined between the development and evolution of psychopathology and TBSA involved (direct relation) or percentage of "disfigurement" [28] (Madianos et al, 2001). Gender and employment are not significant. Psychiatric co-morbidity also appears to be closely related to the clinical-surgical outcome and perception of pain [9,42,12] (DiFede et al, 1997; Perry et al, 1987; Fauerbach JA et al, 2002), and to the length of hospitalization, which may be up to 4 times higher for patients with psychiatric complications following the event compared with those who have none [11] (Falder et al, 2009). These differences with respect to non-psychiatric patients is higher for patients developing drug abuse, followed by ones with psychosis. This difference gradually decreases for patients with mood and personality disorders [54] (Van der Does et al, 1997).

Post-Traumatic Stress Disorder (PTSD)

It cannot be denied that serious burns (TBSA > 25%, 3rd-degree burns) can trigger both acute [10, 30] (< 3 months post-trauma) and chronic PTSD (> 3 months post-trauma) (El Hamaoui et al, 2002) (McKibben et al, 2006).

DSM-IV-TR defines PTSD as a configuration of typical symptoms which become manifest after a person witnesses, is involved in or hears of an extremely distressing fact, which would be traumatic for anyone.

Epidemiology: prevalence is estimated in 1-3% of the general population, although up to 5-15% can suffer a subclinical form of the disorder [35,36,37].

Etiology: a stress factor is needed as a causative event for the development, even if it is not in itself sufficient. Indeed, pre-traumatic factors (biological, social, psychologic) influence

the subjective response to trauma and the proneness of the subject to developing some kind of disorder, more than the intensity of the event itself. Some vulnerability factors which probably play a primary role in determining individual proneness to react to trauma with disorder have been clearly identified [5, 56] (Van Loey NEE et al, 2008).

Table 1. DSM-IV-TR Diagnostic Criteria for Post-traumatic Stress Disorder

A. The person has been exposed to a traumatic event in which both of the following were present:
   1. the person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others
   2. the person's response involved intense fear, helplessness, or horror.
      Note: In children, this may be expressed instead by disorganized or agitated behavior.

B. The traumatic event is persistently reexperienced in one (or more) of the following ways:
   recurrent and intrusive distressing recollections of the event, including images, thoughts, or perceptions.
   Note: In young children, repetitive play may occur in which themes or aspects of the trauma are expressed.
   1. recurrent distressing dreams of the event. **Note**: In children, there may be frightening dreams without recognizable content.
   2. acting or feeling as if the traumatic event were recurring (includes a sense of reliving the experience, illusions, hallucinations, and dissociative flashback episodes, including those that occur on awakening or when intoxicated). **Note**: In young children, trauma-specific reenactment may occur.
   3. intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event.
   4. physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event.

C. Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma), as indicated by three (or more) of the following:
   1. efforts to avoid thoughts, feelings, or conversations associated with the trauma
   2. efforts to avoid activities, places, or people that arouse recollections of the trauma
   3. inability to recall an important aspect of the trauma
   4. markedly diminished interest or participation in significant activities
   5. feeling of detachment or estrangement from others
   6. restricted range of affect (e.g., unable to have loving feelings)
   7. sense of a foreshortened future (e.g., does not expect to have a career, marriage, children, or a normal life span)

D. Persistent symptoms of increased arousal (not present before the trauma), as indicated by two (or more) of the following:
   1. difficulty falling or staying asleep
   2. irritability or outbursts of anger
   3. difficulty concentrating
   4. hypervigilance
   5. exaggerated startle response

E. Duration of the disturbance (symptoms in Criteria B, C, and D) is more than 1 month.

F. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify if:
Acute: if duration of symptoms is less than 3 months
Chronic: if duration of symptoms is 3 months or more
Specify if:
With delayed onset: if onset of symptoms is at least 6 months after the stressor

They are identified with:

1. childhood trauma
2. personality disorders, in particular borderline personality, but also paranoid, antisocial or dependent personality
3. inadequate social or family support
4. genetic-constitutional vulnerability to psychiatric disorders
5. recent distressing changes in everyday life
6. perception of external control
7. recent alcohol abuse
8. several psychodynamic studies have identified alexythimia as a common substrate for patients who have suffered a major psychic trauma.

Some authors identify psychodynamic factors which may explain the genesis of PTSD. Subjects who develop PTSD may not be able to process or rationalize the inductive event, which leads to persistence of the distress and the application of avoidance strategies. Matching their partial ability to face the trauma, patients present alternating periods of recognition or blockage of the event. Some psychoanalytical theorists believe that a previous but unsolved and quiescent conflict may be re-activated by trauma.

Diagnosis. DSM-IV-TR identifies the factors confirming diagnosis of PTSD. The main clinical features are painful re-experiencing of the event, avoidance attitude, emotional paralysis and hyperarousal. The disorder may become manifest months or years after the event. An examination of mental status often reveals feelings of guilt, refusal and humiliation, and panic disorder or an acute dissociative state may also occur [22] (Klein et al, 2006).

Associated symptoms. These may include aggressiveness, violence, limited control of impulsiveness, depression, and drug abuse.

Course and prognosis. PTSD usually develops some time after traumas. The delay may be relatively short - a week, or perhaps as long as 30 years. Symptoms may fluctuate over time and be more intense in stressful periods. 30% of patients reach complete recovery; 40% maintain mild symptoms; 20% moderate symptoms, and 10% show no improvement, or may even worsen. A good prognosis seems to be correlated with quick onset of symptoms, short duration (up to 6 months), good psychical functioning before the disorder, strong social support, and the absence of co-morbidities such as psychiatric or medical disorders or drug abuse. Older and younger patients are usually less able to cope with traumatic experiences. For example, up to 80% of children suffering burns develop PTSD 1 or 2 years after the trauma, versus 30% of adults. A previous psychiatric disability, such as a personality disorder, worsens the effects of distressful situations [5] (Bryant RA et al, 1996). Lastly, those surrounded by a stronger social support network are more greatly protected against the development of the disorder, or develop less severe forms and tend to have better and quicker recovery [27] (Lu MK et al, 2007).

Therapy. The main approaches are support and encouragement to discuss the event, teaching a series of mechanisms for coping with it. Sleeping pills and mild sedatives can often also help, as well as anti-depressants such as imypramine and amytryptiline, which have proved to be effective in both anxiety and reactive depression, with increase of arousal and decrease of avoidance defense mechanisms, negation and emotional paralysis. Some SSRI and other drugs can also be helpful in treating symptoms, especially in the acute phase. A

psychotherapeutic approach (of any school, if suitable to the patient's personality is also of use, and there is also some support for forms of group psychotherapy), These must be the cardinal elements of the approach to these patients, with the aim of inducing them to gradual, supported reconstruction of the event. Lastly, a model of short approach may prove extremely helpful, with support, training, and development of mechanisms to face and accept the negative experience.

Correlations between PTSD and burns [22,47,48]. Although there is no direct relationship between traumas and PTSD, there are patients who are predisposed to PTSD and who must be identified and treated (Taal et al, 1997; 1998) Many studies report the development of PTSD in patients suffering from severe burns (TBSA >25% and 2nd- or 3rd-degree burns) with varying data on prevalence. What emerges is that, compared with other types of traumas, burns may more easily lead to the development of PTSD. Some factors identified as predictive for this are, first of all, scars and changes of the self-image; an avoidance coping style; poor help-seeking behavior; and psychopathology pre-burn [5]. (Bryant 1996)

Some authors speculate whether the development of PTSD is related to patients' reduced ability to react clinically to burns and, even more, to their reduced tolerance to pain, both directly due to the lesions or to medical procedures (dressings, disinfection procedures, operations, etc.) [46] (Taal et al, 1997),

Lastly, poor psychophysical and social prognosis is reported for all patients developing post-traumatic psychopathology, but especially acute or chronic PTSD, compared with patients who have not developed such disorders (Willebrand et al, 2004). The onset of PTSD is thus undoubtedly a negative prognostic factor.

Sleep Disorders

Nightmares

DSM-IV-TR includes nightmares in sleep disorders, particularly in parasomnias. A nightmare is a long dream which evokes fear, so that the subject is frightened on waking up. Like other dreams, nightmares usually begin during the REM phase of sleep, after a long REM late at night. Some people have nightmares frequently in all periods of their lives; for others, they occur mainly during periods of stress or illness. About 50% of the adult population has occasional nightmares. In general, no specific treatment is required. However, when nightmares are a manifestation of an underlying disorder, such as PTSD, it is appropriate to act on the primary disorder, to reduce the intensity and number.

Repeated nightmares are common after burns, although it appears that their frequency decreases with time after the traumatic event. Immediately after burns, nightmares include dominant emotions leading to the event, more than facts directly reminding patients of the trauma. The emergence of nightmares early after burns seems to be predictive for the development of acute or chronic PTSD. Interestingly, some authors have found an association between the onset of nightmares and strategies adopted for coping and reacting to the trauma (Low et al, 2003). Avoidance strategies and re-evaluation/adaptation seem to increase the incidence of nightmares in people who make use of such strategies; conversely, strategies based on emotional and therapeutic, but also affective-family approaches, seem to reduce them.

Women appear to be more prone to nightmares than men, especially if they have neurotic personalities.

Recurring nightmares are one of the criteria for a diagnosis of PTSD and, according to several authors, it indicates the true need to monitor patients, to evaluate the risk of development of acute or chronic PTSD. (Low et al, 2006)

Insomnia

Insomnia is a highly aspecific symptom, common to several medical and psychiatric disorders. In the case of burn trauma, it may be primary or secondary (to pain, nursing, PTSD, procedures, etc.). Insomnia is subdivided into initial, central, terminal and mixed, according to when it occurs during the night. There is no particular clinical difference, but it is important to identify which type is involved, in order to choose the right therapy. Insomnia is a symptom to be evaluated not only for its consequences in terms of control of affections or disorders of ideation and perception (symptoms related to disorders of these functions can indeed be induced by sleep deprivation), but also of the consequences for medical therapy of the primary disorder. For example, insomnia lowers the pain threshold, may cause variations in the response to pharmacological therapy, and lengthens overall healing time.

Table 2. DSM-IV-TR Diagnostic Criteria for Primary Insomnia

A.	The predominant complaint is difficulty initiating or maintaining sleep, or nonrestorative sleep, for at least 1 month.
B.	The sleep disturbance (or associated daytime fatigue) causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
C.	The sleep disturbance does not occur exclusively during the course of narcolepsy, breathing-related sleep disorder, circadian rhythm sleep disorder, or a parasomnia.
D.	The disturbance does not exclusively occur during the course of another mental disorder (e.g., major depressive disorder, generalized anxiety disorder, a delirium).
E.	The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Mood Disorders

Of all disorders of the affective axis, depression is the most frequently reported in burn patients (15-21%) [35, 36] (Palmu et al, 2010).

There is no clinical difference (in terms of symptoms) between major endogenous depression and the depressive episode caused by a traumatic experience. It is accepted that the reaction to an external event is a positive factor for therapy strategies and for the possibility of elaborating the traumatic experience.

A major and necessary distinction is to be made between major depression and a disorder of adjustment to the event which caused the burns, displaying with depressive symptoms.

A disorder of adjustment is by definition directly related to an acute event which happened in the three months preceding onset, and should last no longer than six months after the event. The entity of manifestations is less and the prognosis better compared with typical depression or anxiety disorders. The character of reactivity to a specific event also allows the adoption of a therapeutic strategy which focuses on the elaboration of such an experience.

Table 3. DSM-IV-TR Criteria for Major Depressive Episode

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.
Note: Do not include symptoms that are clearly due to a general medical condition,or mood-incongruent delusions or hallucinations.
   1. depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful). **Note:** In children and adolescents, can be irritable mood
   2. markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)
   3. significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. **Note:** In children, consider failure to make expected weight gains.
   4. insomnia or hypersomnia nearly every day
   5. psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
   6. fatigue or loss of energy nearly every day
   7. feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick
   8. diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)
   9. recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

B. The symptoms do not meet criteria for a mixed episode.

C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

E. The symptoms are not better accounted for by bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

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Delirium

Delirium is an acute and frequent consequence in cases of severe burns, and an average prevalence of 12-13% is reported in burn centers. Delirium is characterized by acute episodes of alteration of consciousness, possible loss of space-time orientation, and alteration of ideation or perception, up to delirium and hallucinations.

These episodes are due to a medical condition which should be investigated, identified and corrected as soon as possible, as it affects the cooperation of the patient to the therapeutical approach and the prognosis.

Table 4. DSM-IV-TR Diagnostic Criteria for Adjustment Disorders

A. The development of emotional or behavioral symptoms in response to an identifiable stressor(s) occurring within 3 months of the onset of the stressor(s).
B. These symptoms or behaviors are clinically significant as evidenced by either of the following:
   1. marked distress that is in excess of what would be expected from exposure to the stressor
   2. significant impairment in social or occupational (academic) functioning
C. The stress-related disturbance does not meet the criteria for another specific Axis I disorder and is not merely an exacerbation of a preexisting Axis I or Axis II disorder.
D. The symptoms do not represent bereavement.
E. Once the stressor (or its consequences) has terminated, the symptoms do not persist for more than an additional 6 months.

Specify if:
Acute: if the disturbance lasts less than 6 months
Chronic: if the disturbance lasts for 6 months or longer
Adjustment disorders are coded based on the subtype, which is selected according to the predominant symptoms. The specific stressor(s) can be specified on Axis IV.
With depressed mood
With anxiety
With mixed anxiety and depressed mood
With disturbance of conduct
With mixed disturbance of emotions and conduct
Unspecified

Table 5. DSM-IV-TR Diagnostic Criteria for Delirium Due to General Medical Condition

A. Disturbance of consciousness (i.e., reduced clarity of awareness of the environment) with reduced ability to focus, sustain, or shift attention.
B. A change in cognition (such as memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established, or evolving dementia.
C. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.
D. There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition.

Coding note: If delirium is superimposed on a preexisting vascular dementia, indicate the delirium by coding vascular dementia, with delirium.
Coding note: Include the name of the general medical condition on Axis I, e.g., Delirium due to hepatic encephalopathy; also code the general medical condition on Axis III.

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Disorders Due to Changes in Self-Image

The effects of burns are not limited to the acute period, but imply a lesser or greater involvement of changes in the self-image, with an influence on functionality and social recovery. Many authors have studied the psychological consequences of scars and bodily disfigurement. Psychical distress is higher in cases in which the burn involved visible body areas, compared with hidden skin, resulting in phenomena of self-exclusion from social life outside the family circle and demonstrating the social dimension of the concept of body image.

The feeling of disfigurement leads to increasing loss of self-esteem, which may trigger a serious depressive disorder.

However, one element which emerges from many studies is the extreme and surprising variability in the frequency of onset of such disorders in the same conditions of trauma. This suggests that what matters most is a subject's self-concept more than the trauma itself and implies that personal elaboration of the presence of scars is the primary element in determining the pathologic or non-pathologic character of the psychiatric reaction.

Again, the concept of intrinsic vulnerability is revealed. A subject without an appropriately solid self-structure is more prone to developing misfit symptoms, due to the changes undergone. The concept adopted in the literature is that of "b*ody image dysphoria*", meaning that a self-image is related, more than to an actual social aspect, to the intra-psychic concept of the body image, which is in turn related to significant others.

The formation of the body image has many components. When it is affected by some kind of disease or disorder, it must consequently be analyzed from different aspects: the dimension of the perception of the self (appearance related to self-esteem and self-concept), a subjective dimension (dissatisfaction, anxiety or distress for how we appear to others) and the dimension of social behavior (distress, avoidance of social activities or of situations which may imply attention to appearance) [24] (Lawrence JW et al, 1998)

A particular problem in these patients may be characterized by the occurrence of Body Dysmorphic Disorder. In some cases, without the true presence, after burns, of scars or bodily defects, some patients develop an exaggerated preoccupation with some particular parts of their body, until they develop clear-cut pathology (and require a very large number of consultations with many specialists, including plastic surgeons).

DSM-IV-TR Diagnostic Criteria for Body Dysmorphic Disorder

A.	Preoccupation with an imagined defect in appearance. If a slight physical anomaly is present, the person's concern is markedly excessive.
B.	The preoccupation causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
C.	The preoccupation is not better accounted for by another mental disorder (e.g., dissatisfaction with body shape and size in anorexia nervosa).

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To conclude, as in the development of other disorders, the psychopathology of the body image also applies the concept of proneness, and a point should be made in identifying

patients at risk, in order to set up procedures for appropriate monitoring, prevention of disorders and care.

CORRELATIONS BETWEEN PRE-TRAUMATIC PSYCHOPATHOLOGY AND BURNS

The presence of truly psychiatric disease (particularly abuse of or dependence on psychotropic substances or alcohol, suicidal behaviour, schizophrenia and (antisocial or borderline personality disorders) is an evident risk factor for those with burn injuries. This is evident from the literature, besides being a commonly reported experience of people working in burn centres.

About 60% of patients admitted for burns have a diagnosis or meet the criteria for Axis I or II psychiatric disorders.

The main psychiatric disorders encountered in burned patients (independently of suicidal ideation or intention, which is often transversal to diagnosis) are:

- Drug abuse/addiction (40%-45% lifetime; 32% before burn);
- Mood disorders (27% lifetime; 6% before burn);
- Anxiety disorder (20% lifetime; 14% before burn);
- Personality disorders - cluster B (18%) [33] (Pagura J et al);
- Psychotic disorder (10% lifetime; 7% before burn);
- Personality disorders - cluster A (8%).

These data clearly show that psychiatric patients should be considered at high risk for burns. This also correlates to suicidal/self-harm intent [16], and in particular to psychotic and personality B cluster disorders, and thus to that percentage of patients who are admitted for self-burn injuries.

In addition, addiction/abuse of drugs limits and complicates the pharmacological approach to clinical, surgical and pain conditions.

Accident Proneness

Besides the existence of post-traumatic psychopathology, it is also true that a traumatic event may happen to a person who has a more fragile and prone-to-trauma personality, or patients with pre-existing psychiatric pathology. In this field too, there is a rich literature.

A number of studies report the increased prevalence of Axis I disorders (pre-trauma) in patients admitted to burn centers. They were suffering from psychotic disorders (mainly schizophrenia), severe depression, alcohol abuse/addiction, and severe personality disorders. Many authors also identify a significant correlation between the presence of such pathologies and more problematic care of burns [11, 12], as the lesions seem to heal less well than those of patients without psychiatric co-morbidity [13, 51]. (Fauerbach et al, 2000; Terrier et al, 2005).

The diagnosis of personality disorder (Axis II) [13, 33] in patients suffering burns is an important element in evaluating the best coping strategy adopt and to anticipate the reaction that the patient will have to the trauma.

Briefly:

- a balanced or neurotic personality will cope with the traumatic experience with a whole, well-defined identity and more numerous and developed psychological defenses (such as removal/repression). In such patients, even in cases of developing psychopathology, preparing a therapeutic approach, and building self-awareness and a therapeutic alliance will be easier.
- people with personality [13,33] disorders or fragile psychical organization display less appropriate intrapsychic functions and will therefore more easily incur psychiatric disorders when a traumatic event triggers the alteration of presumed psychic homeostasis.
- subjects with a psychotic personality structure who cannot easily tolerate any events (even non-traumatic ones), because they feel they are invasive and penetrating for them, and experienced as destructive for their personality [40] (Pavan, 1996).

The above differential diagnosis is important in identifying, evaluating and characterizing accident-prone subjects.

In this sense, the results of some studies examining the epidemiologic distribution of burns in patients admitted to burn centers merit further attention.

Cameron et al [6]. (Cameron DR et al, 1997) studied patients with burns which had been self-inflicted in various ways [37, 34] (Palmu et al, 2004). 16% of these patients were diagnosed as schizophrenic, 39% suffered from severe personality disorders, and 16% major depression, for a total of 58% of patients meeting the criteria for psychiatric disorders [16] (Greenbaum et al, 2004). However, 42% of patients with self-inflicted burns could not be classified under any major psychiatric or personality disorder. In addition, only 50% of those patients had inflicted the burn on themselves in order to commit suicide and, of those, 60% were psychiatric patients, leaving 40% (20% of the total of 37 patients) who had attempted suicide without underlying psychiatric pathology. The remaining 50%, of which more than half suffered from psychiatric disorders, burned themselves not with the aim of committing suicide but for other reasons, which remain unclear.

Malic et al [29] (Malic et al, 2007), in a retrospective study examining 1745 patients admitted to a burn center over a period of 11 years, also found that 4.9% had self-inflicted burns and, of those, only 62.8% suffered from clear-cut psychiatric disorders (depression 33.7%, schizophrenia 7%, affectivity disorders 3.5%, others 17%). The interesting conclusion was that, between the psychiatric patients self-inflicting burns under a defined disorder, and those suffering burns involuntarily, there seems to be a "gray" group which, although not suffering from any defined psychiatric disorder, did burn themselves, and this in itself must involve substantial unidentified suffering.

These are the subjects who are more vulnerable, or accident-prone (suffered or self-procured).

So, "A*ccident proneness*" is defined as a condition in which some subjects undergo a number of events higher than statistically expected as the effect of casuality [3] (Blasco et al,

2003). This concept was first adopted and the term coined around 1920 by Greenwood, who worked on prevention of trauma in occupational health. He had observed that some workers appeared more vulnerable than others, and that if a worker suffered a trauma, he was likely to suffer others in the future. Much attention was then concentrated on the phenomenon, now universally recognized, and many studies have focused on the definition of this process, partly according to a hypothesis of psychological predisposition. One of the most recent studies [3] (Blasco et al, 2003), purely statistical-epidemiological in nature, aimed at evaluating whether the increased incidence of accidental traumas in these subjects is real, and not merely due to casuality. The authors concluded that accident proneness does exist and that it should be attributed largely to the psychical predisposition of the subject.

Concerning the observation of the higher probability of being involved in an accident, once a subject has had one [44] (Poole et al, 1997), this pattern has been identified particularly in subjects suffering from intentional traumas, but it has also been identified in cases of unintentional accidents. Here too the increased incidence of psychiatric comorbidity has been reported, in terms of incidence of major disorders, mainly drug abuse/addiction.

Nonetheless, repeated accidents lead us to hypothesize that the traumas are not necessarily truly casual or independent of the subject's will. Poole stresses the important role which may be played by impulsive acting and the self-destructive traits which can often be identified in these patients.

A similar conclusion regarding the concept and existence of accident proneness was reached by the authors of a recent metanalysis, which gives an univocal definition for the first time [57] (Visser et al, 2007). *Accident proneness* is described as the tendency of an individual (group accident proneness does not seem to exist) to sustain more accidental traumatic experiences than subjects similar in age, gender, occupation, residence, etc., due to stable personality characteristics.

Therapy

Burn patients relate the physical component closely to the psychological component when facing their disorder. The question as to whether physical problems cause more psychological problems, or vice versa, is left unanswered. The correlation between the two is in any case also confirmed by these subjects' relationships with pain and pain perception/tolerance.

Multidisciplinary care of patients with reported burn lesions is therefore essential [55,58,59] (Van Loey NEE et al, 2001; Wiechman Sa et al, 2004; Willebrand M et al, 2004)), not only for clinical healing of the skin, but also for the psychic health of the subject and physical and psychical prognosis at medium/long-term follow-up.

Studies have shown that such multidisciplinary care, together with psychiatric/psychological care by doctors with specific experience of traumas, can:

- prevent clinical relapses;
- shorten the need for hospitalization;
- improve both acute and chronic tolerance to pain;
- improve and facilitate patient care during hospital stays;

- identify high relapse or suicidal actions in at-risk patients (psychosis or abuse);
- help patients to accept their disorder and possible changes in body image;
- contrast the chronicization of some disorders (PTSA) or the onset/persistence of others (major depression, anxiety disorders, etc.).

Treatment of specific psychic aspects may involve:

- specifically psychological therapy, directed at processing of the traumatic experience, changes in body image, return to normal life, and past experiences connected with the traumatic event. This approach may be individual or involve group therapy, depending on the patient, and may require various types of psychological/psychotherapeutic approaches (Cognitive/Behavioral therapy, Focused-problem psychotherapy, Support psychotherapy, Emotional Crisis Psychotherapy, Medium-Long term Psychoanalytic Psychotherapy);
- Pharmacological therapy to treat psychiatric symptoms (decrease in mood pathologic anxiety, onset or worsening of disorders of the ideo-perceptive sphere, insomnia, etc.). Depending on symptoms, the choice will be anti-depressants (TCA, SSRI, NSRI, etc.), mood tone stabilizers, anxiety-reducing drugs, sleeping pills or antipsychotics;
- Handling of possible drug abuse/addiction by specialists.

Our Experience [41]

(Pavan C et al, 2009)

We recently carried out a study evaluating the existence of “accident-prone” subjects among our burn in/outpatients, who had no well-defined diagnosis of major psychiatric or personality disorder. In particular, we examined the more or less conscious potential and subjective conditions or predispositions which may have contributed to the occurrence of the traumatic event, while confirming the absence/presence of psychiatric disorders and assessing the specific characteristics of the subject's disposition and personality.

MATERIALS AND METHODS

25 subjects were recruited from patients admitted to our burn center, Clinic of Plastic Surgery, or Outpatient Clinic for burns or burn sequelae in a ten months period between January 15–October 20, 2007.

Inclusion criteria: men or women, aged 18-65, with 3rd-degree burns with >25% TBSA, minimum 6 weeks and maximum 6 months from inclusion. Patients were asked to agree to participate in the study; they were also required to speak Italian fluently and be able to write without pain.

Exclusion criteria: suicide attempts, psychotic disorders and/or cognitive/sensorial impairment.

The sample population (N=25) was divided in two groups:

- group 1 (N=10): totally accidental involvement: if they had not been at that point at that precise moment, the event would have occurred in any case.
- group 2 (N=15): more or less "conscious" involvement in the cause of the event.

General assessment (patient data, history, causes, source, sites, extension, depth, evolution and treatment undergone) was performed by collecting case-histories from case records and charts and interviewing personnel who had been in contact with the patients.

Psychiatric evaluation was based on:

a. acquisition of clinical history from the patient;
b. Mini-International Neuropsychiatric Interview (MINI) for Axis I diagnosis. For diagnosis of PTSD, we adopted the definition of Stein et al.: presence of at least one symptom per cluster, without the requirement of the presence of all criteria.
c. Paykel Life Events Scale (1973): patient were asked if, in the last 6 months or year, independently of the burn, they had undergone experiences they considered traumatic and/or distressing, with reference to a list (major street accident, violence or aggression, positive or negative changes at work/school, disease – personal or family, separation/break-up/change in affective relationship, problems/improvements in economic/financial matters, major conflicts with another individual, death of important person, problems with the law, others).
d. Hamilton Rating Scale for Depression (HDRS), to evaluate the presence and gravity of depression [scores of less than 8 are normal, between 8-15 mild depression, 16-24 moderate depression, >25 severe depression; clinical cut-off: HDRS>8].
e. State-Trait Anxiety Inventory – Y form (STAI-Y), to evaluate present symptoms of anxiety or anxious personality [45] (Spielberg et al, 1983).
f. Tridimensional Personality Questionnaire (TPQ) [7, 8], (Cloninger, 1987; 1991) for disposition and personality, through evaluation of three areas and sub-areas: 1- NS (novelty-seeking) divided into NS1 (exploratory excitability/stoic attitude); NS2 (impulsivity-reflection); NS3 (extravagance/reserve); NS4 (disorganization/ hyperorganization)(2- HA (harm avoidance) with HA1 (anticipatory anxiety/disinhibited optimism); HA2 (fear of uncertainty/lack of self-confidence) ; HA3 (diffidence toward others/sense of socialising); HA4 (fatigue and weakness/ energy)); 3- RD (reward dependence) with RD1 (sentimentalism/insensitivity); RD2 (ostination/indecision); RD3 (attachment/detachment); RD4 (dependence/ independence).
g. Toronto Alexithymia Scale (TAS-20) [4,39] (Bressi et al, 1996; Parker et al, 2003;) evaluation of alexythimia through: 1- difficulty in identifying emotions and distinction from somatic distress; 2 - difficulty in expressing emotions to others; 3- outward-projected thought.
h. Impact of Event Scale (IES) [18, 43] (Horowitz et al, 1979; Pietrantonio et al, 2002), evaluation of the impact of the burn event on patient's life, based on subscales Intrusion and Escapement.
i. Barratt Impulsiveness Scale, version 11 [14] (BIS-11) (Fossati et al, 2001);
j. Multidimensional Perceived Social Support Scale (MSPSS) [61] (Zimet et al, 1988): evaluation of social support as perceived by the patient: ad: factor 1: relationship

with friends, factor 2: relationship with family, factor 3: relationship with other subjectively important people.

Statistical Analysis

Descriptive statistics were used to evaluate the sample. Fisher's χ^2 test was adopted for categorical variables and Student's t-test for linear variables. In the case of non-linear variables, as defined by the Kolmogorov-Smirnov test, the Mann-Whitney U-test was applied, with Bonferroni correction. Data processing was carried out with SPSS Statistics.15 software.

RESULTS

Socio-Demographic Factors

Total sample is composed by 13 women, 12 men (in group 1, 60% are men and 40% women; in group 2, 40% are men and 60% are women) ($\chi^2$with Fisher's correction =.92, p=.28); average age in group 1 is M±DS 37.9 ± 5.8 and group 2 is M±DS 43.6 ± 16.6 (F=1.096, p=.306).

Type and Characteristics of the Event

Burns affected the face (group 1 40%, group 2 60%), trunk (41.7% vs. 58.3%), upper limbs (60% vs 40%) and lower limbs (37.5% vs. 62.5%).

In group 1, 70% of burns were due to flames and 30% hot liquids; in group 2 80% flames and 20% liquids. TBSA was 33.5% in group 1 and 36.7% in group 2.

Mini International Neuropsychiatric Interview (MINI)

Apparently, psychiatric disorders were more represented in group 2 than in group 1.

In group 2, identified disorders were: severe depression – lifetime (50% of subjects vs 40%); specific phobia (26.7% vs 10%); present PTSD (26.7% vs 20%); partial PTSD following burn (6.7% vs 1%); chronic PTSD (6.7% vs 0%); generalized anxiety disorder (20% vs 0%).

Group 2 revealed present obsessive-compulsive disorder (20% vs 10%) and lifetime one (10% vs 10%); and lifetime drug abuse (10% vs 6.7%).

With regard to PTSD, 40% of group 1 subjects presented with intrusive symptoms, versus 60% in group 2; patients with symptoms of escapement had the same percentages. Symptoms of hyperactivity were identified in 33.3% of group 1 patients and 66.7% of group 2.

Group 2 patients also differed from those of group 1 in higher numbers of traumatic lifetime experiences. They also reported past recourse to psychotherapy (6.7% vs 0% in group

1) and psychiatric drugs (13.3% vs 10%), although the difference was not statistically significant (df=1, χ^2=.626, p=1).

Hamilton Depression Rating Scale (HDRS) [17]

Apparently, group 2 had more severe depression than group 1, but the difference was not statistically significant. Two subjects in group 1 and three in group 2 had scores above the clinical cut-off of 8 (χ^2=.00; p=1).

State-Trait Anxiety Inventory (STAI) [45]

State anxiety seemed to predominate in group 2 (M±SD=41.54±10.12) compared with group 1 (M±SD=30±8.19) (F=7.36, p=.014), as well as trait anxiety (M±SD=38.67±9.43) versus (MD±SD=31±7.11) (F=3.44, p=.081,).

Tridimensional Personality Questionnaire (TPQ) [7, 8]

Significant differences emerged for subscale NS2 (Novelty-seeking; impulsiveness vs reflectiveness) with higher scores in group 2 (F=7.22, p=.015), and for the RD Reward Dependence scale, with higher scores in group 1 (F=3.86, p=.064).

Group 2 had more than double average scores on the NS2 subscale - group 1 (M±SD=1.37±1.18) vs group 2 (M±SD=3.3±1.79), with F=7.22 e p=.015. Instead, group 1 had higher scores in subscale RD4 (M±SD= 4.37±1.18, for group 1, M±SD=3.15±1.34 for group 2 (F=4.44 e p=.049).

Impact of Event Scale (IES) [18, 43]

On the Intrusion subscale, group 1 had lower average scores than group 2 (M±SD=13.5±6.2 vs M±SD=17.2±7.6; F=1.3, p=.25). Also for the Escapement subscale, group 1 results were slightly lower (M±SD9.6±6.1 vs M±SD=11.1±5; F=.38, p=.54), although the differences did not reach statistical significance.

Barratt Impulsiveness Scale vers. 11 (BIS_11) [14]

A significant difference emerged, as group 2 subjects had higher scores (M±SD=64.46±7.51) than group 1 (M±SD=48.88±5.91); F=24.7, p=.000.

Toronto Alexithymia Scale (TAS-20) [4]

Also on the TAS, group 2 had higher but not significantly higher scores in factor 2 – expression of emotions to others (M±SD=12.88±5.37 vs 16.38±3.59, F=3.25, p=.087) (Bressi et al, 1996).

Multidimensional Perceived Social Support Scale (MSPSS) [61]

No significant differences emerged, although group 1 patients tended to perceive stronger social support.

Paykel Life Events Scale

In this test too, no significant differences emerged, although group 2 patients had a slightly higher incidence of events in the last 6 months (U=62; p=.46).

DISCUSSION

In general, our study revealed a tendency toward a higher incidence of psychopathological features in group 2 than in group 1. However, the two features in which differences were statistically significant were the Barratt Impulsiveness Scale, and subscale NS 2 of TPQ, both of which are related to impulsiveness.

The MINI semi-structured diagnostic interview, with variable frequency, detected the more frequent presence of psychiatric disorders in group 2, particularly severe depression (lifetime), alcohol abuse (lifetime), special phobia (present), disthymia, panic attack disorder (present and lifetime), agoraphobia, drugs abuse, PTSD (present, following burn). Co-morbidities, which were not statistically analysed, but which probably played an important clinical role, were also frequent.

The presence of psychiatric disorders in group 2 patients does match the results of other surveys, both in burn patients (pre-trauma psychopathology), and in patients treated for self-inflicted burns [13,29,51,60] (Fauerbach et al, 1996, Malic et al, 2007; Terrier et al, 2005; Zarghami et al, 2002). According to this evaluation and to the literature, group 2 patients may therefore be more disposed to traumas in some way.

It was noted that these patients also had recourse to psychopharmacologic and/or psychotherapeutic treatment, which indicates that the pre-trauma experience had been sufficiently important to induce them to ask for help.

Unlike reports in the literature, our patients showed a tendency to higher prevalence of obsessive-compulsive disorder (present and lifetime) in group 1. This is difficult to explain by clinical reasoning, as it may be presumed that subjects with obsessive-compulsive disorder would be more prone to illogical and dangerous behavior, while not thinking about the consequences of their actions. Conversely, compulsion is a programmed and deeply-thought-out action - an aspect which excludes impulsiveness. This may merit further investigation.

Group 2 was also more prone to anxiety disorders, both present (perhaps due to recent trauma) and of trait, and thus more linked to temperament. This has been confirmed by other studies, in particular in patients admitted for self-inflicted burns. The *STAI index* apparently identifies a more important anxious state in such patients than that which emerges with the MINI.

Of high value were the results emerging from the *Barratt (11)*. This scale of impulsiveness quantification revealed a highly significant difference between the two groups, group 2 patients having higher impulsiveness than group 1.

Impulsiveness is a predisposition to quick, unexplainable actions after both internal and external stimuli, without reasoning or analysis of the consequences for the person involved or for others. It is not a synonym of aggressive behavior but a predisposition; it also differs from compulsion, which always follows deep programming of the action. It is involved in many psychiatric disorders, both in the pathogenesis of some behaviors or as the expression of temperament: in antisocial personality disorder, borderline personality disorder, drug abuse, and bipolar disorder. As a symptom, it may be transversally present in many disorders, beyond those mentioned above.

Treatment of this temperamental aspect is closely related to social, biological and psychological causes. The logical consequence is that, to treat these alterations, a multi-disciplinary therapeutic strategy must be created.

However, many studies have noted that most expressions of impulsiveness in psychic distress appear in the form of aggressive actions or feelings. This may lead to actions which are dangerous for the subject or for those sharing relations or living space, and which should be taken into adequate consideration.

As in other studies, we note the importance of instruments for evaluating impulsiveness [31, 32] (Moeller et al 2001), and the inadequacy of most methods. The Barratt behavioral scale (Barratt, 1993, 1998) seems to be a broadly accepted and effective method. Barratt believed that the best solution for developing an "impulsiveness index" unifying biological-social-behavioral and ambient aspects, was the relationship between impulsiveness and behavior, unprogrammed actions being an index of impulsiveness [31, 32]

Therefore, concerning the aims of our study, impulsiveness and unprogrammed actions for oneself/others may be important in burn pathology, as group 2 subjects act with an unconscious and unprogrammed aim, unaware that they are falling into major trauma. Measuring impulsiveness and finding higher prevalence in this group has important consequences in understanding the etiopathogenesis of the behavior of these subjects. Higher impulsiveness seems to dispose them to incur burns.

As possible confirmation, the TPQ test, which evaluates the subject's temperament, showed a tendency to higher prevalence of the different aspects in question (disorganization-eccentricity, fear of uncertainty, diffidence, fatigue, etc.) in group 2 patients, particularly with significant differences in the NS2 subscale, which analyses aspects of impulsiveness.

Matching these two results is important, as it suggests that these subjects are not only more prone to traumatic events because of impulsiveness in their actions, but also to a concomitant underlying intrinsic impulsive trait in their personality, of which they may be unaware.

A further element which emerged was the greater frequency of drug and alcohol abuse, largely confirmed in the literature as pre-burn psychopathology, and perhaps connected with the more or less programmed actions and behavioral traits.

Although not reaching significance, the trend of more frequent traumatic experiences lifetime in group 2 may be important, as it seems to support the hypothesis of "accident proneness", which may lead to a chain of traumatic experiences progressively and exponentially increasing the subject's vulnerability.

The two aspects are interconnected, as if, on one hand, the accumulation of internal or real traumas can increase vulnerability and make the subject accident-prone. On the other, the acting of the subject, in which we see impulsive temperament and behavior, increases the risk of incurring traumas or distressing events which may alter intrinsic equilibrium.

Interestingly, the post-traumatic response of group 2 subjects, who developed PTSD, was more oriented toward intrusiveness and escapement, as if, the impulsive action leading to burns being unprogrammed, coping with the event was also more difficult. This is like saying that a temperamental vulnerability unconsciously induces the trauma, which subjects later do not want to face by processing the experience, but wish to avoid or leave free to intrude massively in their minds.

Group 1 patients also tend to have more social/family support (*MSPSS*) [38] (Park et al, 2008). This may result in a protective factor, both internally and practically, and also mirror a personality more prone to seeking relationships. Instead, the more deficient social network of group 2 patients may be due to their inferior seeking of contacts or to greater difficulties in building and maintaining relationships, in turn attributed to their impulsive personality traits. However, these are only speculations which need further investigation and confirmation with other instruments.

In this study, personality was not investigated through specific instruments. However, one aspect was analyzed by the TAS-20 (*Toronto Alexithymia Scale)* [1, 2] (Bagby RM et al, 1994), which showed a tendency to higher scores in group 2 (factor 1: difficulty in identifying emotions and distinguishing them from a physical disturbance; factor 2: difficulty in expressing emotions).

Alexithymia has long been recognized as a possible personality construct which acts as a risk factor in a number of psychiatric and psychosomatic disorders. Until now, the TAS-20 has been one of the best tests of this aspect, connecting it to the three factors it involves and the related personality disorders. Alexithymia (secondary) may be a symptom of depression, a praecox expression of cognitive disorders, or present with panic attacks and eating disorders, and studies reveal a close association with PTSD as the incapacity to express emotions after an event felt as traumatic.

However, many studies have also characterized alexithymia as the expression of a primitive trait of the subject's personality. In this case, it may be the expression of any personality with pathologic tendency, with different meanings: the alexithymia of a psychotic personality is exalted in its introversive aspects, "neurotic" alexithymia has a strong accent of emotional emergency, while in extroversive personalities it manifests as the incapacity to perceive positive emotional intensity [1, 2].

The two aspects may coexist, with secondary alexithymia developing on a background of primary alexithymia, as the result of trauma. This is important in approaching the patient, as it may influence the risk of expression of other psychopathologies or of non-metabolized trauma reiteration [62] (Zimmermann et al, 2008). Such analysis was not possible in the present study. But the topic merits further investigation.

Limitations

This study explores the nature of the relationship between impulsiveness and the predisposition of some subjects to burn trauma. However, it has some limitations. The hypothesis assumed in the study design was that, in group 2 patients, the event was more or less consciously self-inflicted, introducing a non-casual component into the causality of burns. This choice of categorization is subjected to the risk of False Negative/False Positive errors (over-estimated or under-estimated intentionality). The limited number of the study groups may be why some differences emerging between the two groups showed a trend but did not reach statistical significance. The fit of these trends with other statistically significant results observed indicates that the subject merits further attention and deeper investigation.

It may also be of great interest to undertake a long-term follow-up of these patients, to study the clinical and psychopathological evolution of burn trauma, with its influence on life quality.

CONCLUSION

Overall, this study reveals that some burn patients present high pre-burn levels of impulsiveness and pre-morbid psychopathology. These patients are more prone to developing PTSD, and they develop it with more symptoms

Such levels of impulsiveness and psychopathology not openly severe (psychosis, borderline personality disorders, severe depression) in these patients seem to confirm our hypothesis of accident proneness in comparison with group 1 patients. Strategies to identify these patients should be identified, and an approach based on the importance of attempts to prevent this disorder should be considered and developed.

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