Scar Management in the Pediatric and Adolescent Populations

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For most children and adolescents who have developed symptomatic scars, cosmetic concerns are only a portion of the motivation that drives them and their caregivers to obtain treatment. In addition to the potential for cosmetic disfigurement, scars may be associated with a number of physical comorbidities including hypertrichosis, dyshidrosis, tenderness/pain, pruritus, dysesthesias, and functional impairments such as contractures, all of which may be compounded by psychosocial factors. Although a plethora of options for treating scars exists, specific management guidelines for the pediatric and adolescent populations do not, and evidence must be extrapolated from adult studies. New modalities such as the scar team approach, autologous fat transfer, and ablative fractional laser resurfacing suggest a promising future for children who suffer symptomatically from their scars. In this state-of-the-art review, we summarize cutting-edge scar treatment strategies as they relate to the pediatric and adolescent populations.

Any significant injury to the deep dermis, such as burns and other trauma, inflammation, or surgery, may result in wound healing that presents clinically with the formation of a scar. ¹ Much time and energy has been spent attempting to classify scars on the basis of histopathology or clinical morphology. Although doing so is useful for documentation and management decisions, it belies the reality that a scar by itself is neither “good” nor “bad.” Scars are simply the clinical end point of a confluence of genetic and environmental factors affecting the wound-healing process after a cutaneous insult. From the perspective of human history, most serious wounds have been traumatic (eg, “tooth and claw,” falls, burns, combat), involving widespread areas of damage that needed to be contained quickly and efficiently to control bleeding and infection. It is only relatively recently that iatrogenic (ie, surgical) scars have begun to strongly influence the discussion of what type of scar is “acceptable.” Any scar can be symptomatic, and even clinically benign-appearing scars may cause a patient physical, psychological, and social comorbidities leading to severe impairment of quality of life.² To label 1 type of scar “pathologic” and another “normal” by virtue of morphology or histopathology alone misses this point.

Each year ∼100 million individuals acquire scars after an estimated 55 million elective operations and 25 million operations after trauma in the developed world. Within this larger group, there are an estimated 15 million keloids and hypertrophic scars per year, an estimated 70% of which occur in children.³ The dramatic increase in the survival rate of pediatric patients suffering from severe burns in the past several decades has translated into an increasing number of children left to...
deal with disabling and disfiguring scars.4

With the high scar prevalence in the pediatric population and the associated physical, psychological, and social comorbidities, there is a need to enhance understanding and management of scars among health care providers. Goals of therapy for any scar should be established in conjunction with the individual patient and, at a minimum, should focus on relieving symptoms, reducing comorbidities, decreasing scar volume, and maximizing functional and cosmetic outcomes. In this state-of-the-art review, we summarize current cutting-edge scar treatment strategies as they relate to the pediatric and adolescent populations.

SCAR MORPHOLOGY

Several clinical and histopathological classifications may be useful in a discussion of scar management (Table 1). Atrophic scars appear as concave depressions in the skin and result from net loss of tissue, including collagen. Atrophic scarring may be observed in association with a variety of conditions such as acne, striae, discoid lupus, varicella, molluscum contagiosum, malignant atrophic pustulosis (Degos disease), infections (especially *Staphylococcus*), surgery, and trauma (Fig 1). Matrix metalloproteinases (MMPs) assist the remodeling process by degrading a variety of extracellular matrix proteins. A simplistic concept of atrophic scar formation is a relative shift in the ratio of MMPs to tissue inhibitors of MMPs, resulting in a lytic cascade that favors an atrophic scar.5

In contrast, hypertrophic scars and keloids result from net gain of collagen deposition. Hypertrophic scars remain within the boundaries of the precipitating insult and typically develop relatively soon after injury to the deep dermis. Keloids, in contrast, extend beyond the boundaries of the original injury and often have a delayed onset of development. Keloid formation typically affects dark-skinned individuals (Fitzpatrick IV–VI skin type), with the majority of keloids manifesting in persons 10 to 30 years of age.2,6,7 Younger children are still susceptible, however, as bilateral earlobe keloids have been documented in a 9-month-old African American girl 6 months after piercing.8 In addition to differences in clinical appearance, keloids often differ histopathologically from hypertrophic scars in a variety of ways, with the most distinguishing feature being the presence of thickened hyalinized collagen (keloidal collagen).3 Keloid formation has also been associated with a family history of keloids, hyper-immunoglobulin E syndrome, blood type A, and hormone peaks during puberty and pregnancy.10–13

PHYSICAL SIGNS AND SYMPTOMS

Objectively, scars may appear erythematous, a likely function of the scar’s newly formed vascular network that may serve as an indicator that the scar has entered the active remodeling/maturation phase.14 Likewise, a scar may be dyspigmented as a result of disparities in melanocyte concentration and/or melanin production within affected and unaffected tissue. Clinically, this may lead to hypo- or hyperpigmented skin, or both (ie, “mottling”; Fig 2).
Scars may manifest pruritus, tenderness and pain, and dysesthesias, all of which may result in sleep disturbances and disruption of daily activities. These are likely exacerbated by a variety of factors, including local friction, inflammation, stimulation of nerve endings in and around the scar, and increased local levels of B-endorphin. Hypertrichosis within scars has also been reported in postoperative patients with knee replacement surgeries and in patients with surgical scars requiring the use of orthopedic casts and splints. It is postulated that this phenomenon may be secondary to increased friction, vascularity, and local growth factors. Likewise, certain scars may contribute to local hyper- or hypohidrosis, exacerbating skin irritation and maceration in the setting of scar fragility. Cumulatively, these factors may interfere significantly with physical/occupational rehabilitation efforts.

Contractures are a potentially disabling consequence of the scar maturation process, especially after extensive burns and other traumatic injuries. Scar contractures across a joint may lead to a significant loss of strength and range of motion, significantly affecting function and overall quality of life. Contractures along a free edge such as the eyelid or lip may have both a functional and profound cosmetic impact. Patients with suspected function-limiting contractures may be assessed for deficits according to standardized guidelines. This is especially important in the pediatric population, in whom deficits may affect normal development.

Key anatomic locations may be divided into multiple topographical “cosmetic units.” The face, for example, is commonly demarcated into cosmetic units that include the forehead, eyes, nose, lips, chin, ears, and neck, with each of these units further classified into additional anatomic subunits. Aesthetic theory teaches that scars that fall in a single cosmetic unit or at the junction between units tend to be less conspicuous than those that cross boundaries. Consequently, scars that disrupt cosmetic units are often more noticeable and may be more likely to lead to both physical and psychosocial comorbidities.
Issues may manifest as a direct physical consequence, or as an indirect consequence of others’ reactions to the scarred individual (eg, bullying; Table 2).

**PSYCHOSOCIAL SIGNS AND SYMPTOMS**

When caring for pediatric patients with scars, it is important to note that the contribution of psychological and social factors to overall quality of life is frequently underreported and underdiagnosed (Table 2). Clinician-rated scar severity and scar types may not necessarily correlate with the extent of a patient’s psychosocial distress. Indirectly, the reaction of others to a scar may play a crucial role in the stigmatization or discrimination of the affected individual. This may manifest in others as a lack of courteous behavior, staring, startled responses, intrusive questions, avoidance, rude comments, teasing, and bullying. Such behaviors can lead to a sense of rejection, loneliness, isolation, and “social death,” with important implications for social interaction and employment opportunities.

The combination of traumatic burn accidents, laborious and repetitive treatments, and residual disfigurement and dysfunction has been demonstrated to lead to psychopathological responses in children such as depression, separation anxiety disorder, and posttraumatic stress disorder.

As such, >50% of burn-injured children may eventually develop manifestations of posttraumatic stress disorder. For these reasons, a multidisciplinary specialty team may be beneficial when managing patients with disfiguring and debilitating scars.

**STATE-OF-THE-ART SCAR MANAGEMENT**

A recent proliferation of research in scar therapeutics parallels the recognition of the impact of treatment beyond cosmetic appearance alone. This is particularly relevant in pediatrics, in which utility must often be extrapolated from adult studies and the profound physical and psychological implications associated with scarring (such as the seemingly ubiquitous atrophic scarring secondary to acne) mandate a consideration of multimodal treatment options. Although a wide range of “conventional” options (Supplemental Information) reflect the inconsistent and frequently disappointing efficacy of traditional therapies, the cutting-edge modalities reviewed herein offer the potential to advance the field of pediatric scar mitigation, revision, and perhaps eventually prevention.

**MULTIDISCIPLINARY MANAGEMENT**

Like in so many areas of medicine, scar prevention and mitigation are preferable to treatment of an existing symptomatic scar. Scar mitigation begins with coordinating and optimizing procedural technique and other factors such as keeping...
wounds moist, timely and judicious wound debridement, minimizing the tension of wound closure, prevention of infections and hematoma formation, avoidance of sun exposure to minimize postinflammatory hyperpigmentation, and maximizing nutritional status. Furthermore, a health care provider’s ability to identify a situation likely to result in symptomatic scar formation is imperative. Certain anatomic locations with high tension such as the shoulder, neck, presternum, and ankle are predisposed to hypertrophic scars. Dark-skinned patients and any patient with a personal/family history of pathologic scar formation should incite humility in any provider contemplating an elective procedure, especially in high-risk locations.

Complex scars may require multiple interventions performed either concurrently or in a step-wise fashion for optimal results. A single provider from a single specialty may not possess the experience or expertise necessary to consider and implement all of the various approaches that may be required. Combining experts from dermatology, plastic surgery, wound healing, trauma/abuse counseling, nutrition, behavioral health, physical/occupational therapy, radiology, and social work, a multidisciplinary scar team may provide more efficient, optimized care to complicated scar patients. This “team” approach has previously demonstrated utility in the management of vascular lesions, cleft lip and palate, and pediatric burns. Larger, prospective studies will shed light on the true effectiveness of this model of scar care as an intervention in and of itself.

**INTRALESIONAL CORTICOSTEROIDS**

Intralesional corticosteroids remain a mainstay in the treatment of hypertrophic scars and keloids, with a response rate of ~50% to 100% and a recurrence rate of 9% to 50% for keloids in 1 review. One prospective pediatric study involving 15 patients with earlobe keloids included treatment with an aggressive regimen including preoperative, intraoperative, and postoperative intralesional triamcinolone acetonide suspension as an adjunct to keloid excision. Of the pediatric patients who adhered to the regimen, none showed signs of keloid recurrence at 6 months of follow-up, with a single recurrence noted at 18 months of follow-up. The efficacy of corticosteroids for these types of scars is likely secondary to their ability to suppress inflammation, promote collagen degeneration, inhibit collagen production, and limit wound oxygenation and nutrition.

The optimal number of treatments has yet to be determined, and dosing for intralesional scar therapy varies depending on lesion characteristics and anatomic location. Local cutaneous atrophy and hypopigmentation are the most common side effects of therapy. Pain on injection may be a significant obstacle to use in pediatrics, with 1 study showing an attrition rate of nearly 1 in 3 despite significant efficacy in the treatment of facial keloids. Topical lidocaine cream before injection may help minimize discomfort. Triamcinolone acetonide injectable suspension contains benzyl alcohol, which has been reported to cause toxicity in neonates, particularly in small preterm infants. Although exposure is likely negligible in the setting of intralesional use, the amount of benzyl alcohol at which toxicity occurs is not known, and use of this medication is not recommended in neonates.

**INTRALESIONAL 5-FLUOROURACIL**

Five-fluorouracil (5-FU) is a pyrimidine analog with antimetabolite activity that has been shown to inhibit collagen synthesis both in vitro and in vivo. When delivered intralesionally into keloids and hypertrophic scars, 5-FU has demonstrated significant efficacy in several adult studies. A 44-week, double-blind, randomized trial compared intralesional triamcinolone acetonide (40 mg/mL) with 5-FU (50 mg/mL) tattooing every 4 weeks for a total of 12 weeks for the treatment of keloids. Both groups demonstrated improvement in all assessed parameters including erythema, pruritus, height, surface, and induration. However, improvement was more significant in the 5-FU group.

5-FU is considered “off-label” for scars, and its safety and effectiveness in children have not been established, either alone or in combination with intralesional corticosteroid. Adverse effects include pain and hyperpigmentation. It is Pregnancy Category D and may cause fetal harm when administered to a pregnant woman.

**AUTOLOGOUS FAT TRANSFER**

For scars associated with volume loss, the techniques of autologous fat transfer (AFT) and composite grafting offer significant promise. In the pediatric population, AFT has been used in the treatment of facial malformations due to Goldenhar syndrome, Treacher Collins syndrome, and hemifacial microsomia. AFT may offer benefits beyond volume replacement, with graft components mediating a dynamic remodeling process that may accelerate revascularization and decrease fibrosis after thermal injury. Combinations of AFT with ablative and nonablative fractional laser resurfacing and platelet-rich plasma have also been demonstrated to enhance scar treatment.
**SURGICAL EXCISION**

Surgical excision may prove useful in cases in which conservative therapies alone have failed to yield significant improvement. As monotherapy, excision of keloids has a dismal recurrence rate that may approach 100%.60–62 Consequently, excision is typically performed in combination with adjunctive perioperative modalities, which may help reduce the risk of recurrence.63,64 In 1 study that included patients ranging from 11 to 79 years of age, excision of pathologic scars followed by a corticosteroid injection every 2 weeks (for a total of 5 injections) along with self-administered steroid ointment application twice daily for 6 months, showed a recurrence of keloids in 14.3% of cases and a recurrence of hypertrophic scars in 16.7% of cases.65

**SURGICAL REVISION**

Surgical revision may be required for debilitating scar contractures refractory to physical/occupational therapy and other more conservative measures. Surgical techniques include scar-lengthening flaps, excision, and skin grafting, which may be delayed for a year or more to allow for spontaneous scar maturation. This delay has been built into most scar treatment paradigms because surgical treatment itself is associated with additional morbidity and relatively high recurrence rates.60,62 Traditional surgical techniques for contractures include Z- and W-plasties; the former is a scar lengthening procedure that relieves tension and decreases contracture to help improve range of motion, and the latter helps render lengthy linear scars irregular and less discernable66,67 (Fig 5).

**LASER SURGERY**

Lasers such as the vasculature-targeting 595-nm pulsed dye laser and the full-field ablative 10 600-nm CO₂ laser continue to be effectively integrated into the treatment of various scar types. These modalities are, however, somewhat limited in large traumatic scars because of modest efficacy and excessive thermal damage, respectively.30,68–70 Treatment with pulsed dye laser is based on selective photothermolysis, with hemoglobin serving as the target chromophore. Moderate damage to local blood vessels results in a remodeling response that can help reduce scar erythema, pain, itch, and prominence71–76 (Fig 6).

Some of the most exciting recent advances in scar treatment are associated with the emergence of fractional photothermolysis in 2004.77 This involves the generation of a pixelated pattern of narrow columns of thermal injury (vaporization or coagulation of tissue) in the treatment area, based on the heating of tissue water. Fractional lasers are the first to offer a selectable depth of penetration, up to several millimeters. The tissue response to laser-induced thermal injury shares some common features with wound repair. An early inflammatory response is followed by cell proliferation, MMP-guided turnover of extracellular proteins, and long-term neocollagenesis and dermal remodeling.78–80 In the case of fractional ablative laser treatment, vigorous remodeling appears to eventuate in scar tissue with a dermal architecture and ratio of collagen subtypes closer to that of normal skin.81 The combination of treatment depths unavailable to previous devices with an adjacent undamaged reservoir of viable tissue is likely responsible for the observed safety and efficacy of treatment, which has established a new gold standard in
The recent observation that ablative fractional laser resurfacing can objectively improve function and enhance rehabilitation in the pediatric and adult populations has profound implications for current paradigms in traumatic scar management (Fig 7).

Relatively few safety reports involving fractional laser scar treatment in the pediatric population exist in the literature, although there is largely anecdotal evidence that fractional laser therapy is well tolerated with a low rate of complications. Lasers can be associated with significant discomfort during treatment, which is an important consideration for pediatric patients. Topical anesthetics, local intradermal injection, regional nerve block, oral and intravenous sedation, and general anesthesia have all been successfully used in laser therapy for this population.

**LASER-ASSISTED DELIVERY OF MEDICATIONS**

The use of topical corticosteroids has traditionally been discouraged in scar management because of a lack of efficacy and risk of epidermal atrophy. Numerous strategies have been attempted to enhance topical drug delivery through fibrotic scar tissue. The technique of laser-assisted delivery (LAD) takes advantage of temporary barrier impairment induced by various ablative and nonablative fractional photothermolysis technologies; it pairs topically applied medications with laser therapy to increase penetration and absorption of the applied agents (Fig 8).

Although the number of published articles on the use of this technique in pediatrics is limited, several reports demonstrate the potential utility of...
such an innovation. One prospective case series involving 15 subjects with hypertrophic scars reported the use of ablative fractional laser followed by immediate topical application of triamcinolone acetonide (10–20 mg/mL depending on location and thickness of the scar). The subjects underwent 3 to 5 treatment sessions at 2- to 3-month intervals. At the end of the study, scar texture showed the most improvement, whereas dyschromia showed the least amount of improvement.96

A second prospective case series treated 4 subjects with hypertrophic scars by using ablative fractional radiofrequency followed by topical triamcinolone acetonide 20 mg/mL. Acoustic pressure ultrasound helped “push” triamcinolone molecules through the ablated microchannels. Complete resolution of the treated scar was noted in as little as 1 session for lesions on the nose and mandibular area, with significant improvement in all areas of the body after 4 treatment sessions.

A potential disadvantage of LAD is that many topical medications have not been evaluated for this route of application, and patients may experience side effects seen in either or both topical medication administration and laser surgery. Likewise, LAD may increase penetration of not only the desired medication but also any excipients applied to the treated field; sterility and unintended side effects must be considered with this fact in mind.97

ON THE HORIZON

Our understanding of the pathophysiology of scar formation and fetal wound healing continues to accelerate. The recent elucidation of the role in scarring that engrailed-positive fibroblasts, which express CD26 on their surface, play is an example of how far scar-related basic science has progressed; the possibility that medications such as sitagliptin and vildagliptin, oral antihyperglycemics used in the treatment of type 2 diabetes mellitus, may actually inhibit this specific lineage of fibroblasts lays the groundwork for a true paradigm shift in the field.98 Such discoveries allow for the exploration of more specific therapeutic options for scars and, perhaps, may lead to future applications in scarless wound healing.

REACTIVATION OF FETAL PATHWAYS

Before the end of the first trimester of gestation, human fetuses do not follow the traditional “inflammatory cascade” model of wound healing. Instead, early fetal wound healing is characterized by a relative paucity of inflammatory cell activity and reactivation of developmental pathways. The end result appears to be true tissue regeneration without scar formation.99 How humans transition from reactivation/regeneration to the traditional inflammatory model of wound healing has yet to be demonstrated. However, not all mammals lose this ability. The African spiny mouse appears to regenerate hair follicles, sebaceous glands, dermis, adipose tissue, and cartilage from deep cutaneous injuries even in its adult life.100 Elucidating these fundamental mechanisms of wound repair promises to inform future therapeutic modalities, and perhaps even reintroduce scarless healing.101,102

STEM CELLS

Stem cells are a promising source for novel therapies in scar treatment and tissue repair. The presence of induced pluripotent stem cell-conditioned medium appears to reduce levels of type I (adult) collagen and attenuates the local inflammatory cell response in vitro.103 Additionally, mesenchymal stromal cells may have the ability to be reprogrammed into sweat gland-like cells, offering the potential to restore injured adnexal structures from deep burn injuries.104

AUTOLOGOUS FIBROBLASTS

In a randomized, multicenter, double-blind, placebo-controlled trial,
subjects with bilateral, moderate to severe acne cheek scarring treated with a series of unilateral autologous fibroblast injections had a statistically significant improvement on blinded photographic evaluation compared with placebo-treated controls 4 months after their final injection. Trials are currently underway to see if similar interventions can improve scar pliability, improve range of motion, and restore function in contracture scars.

INTERLEUKIN-10

Interleukin (IL)-10 is an antiinflammatory cytokine highly expressed in midgestation human fetal skin but absent in postnatal human skin. In fetal regenerative wound healing, IL-10 is believed to play a prominent role because it has been shown to deactivate macrophages and neutrophils while also diminishing the production of proinflammatory cytokines IL-6 and IL-8. Furthermore, IL-10 levels and fibrotic processes appear inversely correlated in postnatal tissue repair. Recently, 2 murine studies and a phase II randomized controlled trial in humans have confirmed the importance of IL-10 in reducing inflammation, accelerating wound healing, and reducing scarring with the use of exogenous recombinant human IL-10 application to cutaneous incisions, suggesting that rhIL-10 may be a new class of therapeutic options for scar minimization.

TRANSFORMING GROWTH FACTOR-β

Transforming growth factor-β (TGF-β) is thought to be an important growth factor in scar formation. In general, TGF-β1 and TGF-β2 physiologically promote fibroblast proliferation and collagen production in the proliferative phase of normal wound healing and have been found to be overproduced and unregulated in keloidal tissue. In contrast, TGF-β3 appears to function as a scar inhibitor.

Animal studies have demonstrated promising results with topical application of TGF-β1 and TGF-β2 antagonists resulting in expedited reepithelialization and reduced scar formation and wound contraction in partial-thickness/full-thickness porcine burns as well as in rabbit skin excision models. In addition, application of recombinant TGF-β3 has been shown to reduce scar size. Recombinant TGF-β3 appears to be useful for prophylaxis against and treatment of surgical scars.

BASIC FIBROBLAST GROWTH FACTOR

Basic fibroblast growth factor (bFGF) is an important cytokine that activates macrophages and plays a crucial role in early wound healing. In 1 controlled adult study, topical bFGF resulted in better scar quality and accelerated wound healing.

The potential for therapeutic use of bFGF has been studied in the pediatric population. One study showed that children with second-degree burns who received topical bFGF had a significantly enhanced skin/scar color match compared with the placebo group that received only impregnated gauze after 1 year. Furthermore, hypertrophic scars developed in 0 of 10 wounds in the bFGF treatment group compared with 3 of 10 wounds in the control group. Parameters such as effective contact coefficient, transepidermal water loss, water content, and scar thickness were also significantly greater in the control group ($P < .01$). Further prospective, randomized, controlled clinical studies are needed to establish the safety and efficacy of bFGF for its potential role in scar therapy.

MMPS

MMPs play an important role in tissue remodeling by degrading extracellular matrix components, growth factors, cytokines, and additional proteases. Studies have demonstrated increased MMP-1 expression, through either a therapeutic factor or direct application of purified MMP-1, may have a beneficial impact on hypertrophic scars.

CONCLUSIONS

Myriad management options for symptomatic scars exist, with no universal consensus on what constitutes the safest and most efficacious treatment modalities. Even less is certain regarding the pediatric and adolescent populations because of a lack of controlled trials within these age groups. Symptomatic scars remain a challenge for both the patients who must live with them and the health care providers who are asked to manage them. Nevertheless, much progress has been made in the past several years, with combination therapy yielding tremendous clinical improvements. The emergence of scar therapies that target specific molecular and cellular pathways represents a promising future in scar management and, possibly, even scar prevention.

ABBREVIATIONS

- 5-FU: five-fluorouracil
- AFT: autologous fat transfer
- bFGF: basic fibroblast growth factor
- IL-10: interleukin-10
- LAD: laser-assisted delivery
- MMP: matrix metalloproteinases
- TGF-β: transforming growth factor-β
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