Advances in scar management: prevention and management of hypertrophic scars and keloids

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Purpose of review
Abnormal scarring remains a poorly understood but functional and aesthetic consequence of surgical and traumatic wounds. The purpose of this review is to describe the current state of the science behind the prevention and management of these scars.

Recent findings
A recent update in the International Clinical Recommendations on Scar Management provides a wealth of information on new and revised treatments for hypertrophic scars and keloids. Silicone-based products continue to be the premier option for prevention and initial treatment of hypertrophic and keloid scars. There is growing evidence demonstrating the efficacy of intralesional corticosteroids and 5-fluorouracil. Laser therapy remains a second-line treatment option, with low-level evidence supporting the use of pulse dye lasers and ablative fractional lasers.

Summary
Although there remains no ‘gold standard’ for the prevention and treatment of hypertrophic scars and keloids, silicone gel products and microporous paper tape present the best conservative options. A stepwise algorithm for the treatment of hypertrophic scars or keloids based on the characteristics and responsiveness of the scar presents the best management strategy. Combination therapy (including steroid injections, 5-fluorouracil, and pulse dye laser) proves to be the strongest option for the nonsurgical management of severe hypertrophic scars and keloids.

Keywords
5-fluorouracil, hypertrophic scar, keloid, silicone sheeting, steroid injection

INTRODUCTION
Hypertrophic scars and keloids remain a challenging aesthetic deformity to manage because of high rates of recurrence and a multitude of treatment options. Abnormal healing processes can result in these proliferative scars after even minor traumatic and iatrogenic wounds. Hypertrophic scars are often the result of surgical wounds or burns and more commonly seen in lighter skinned individuals. They appear red, raised, or itchy and remain within the boundaries of the wound. Keloid scars are seen in darker skinned individuals and characterized by their extension beyond the boundaries of their original wound and propensity to recur [1]. They can be categorized as minor or major keloids, with major keloids being larger, more raised (>0.5 cm), and painful [2**]. In addition to their clinical presentation and gross appearance, these scars demonstrate histologic differences. Although keloids contain disorganized bundles of types I and III collagen, hypertrophic scars are comprised of well-organized type III [3]. Thus, hypertrophic scars and keloids merit different treatment approaches and management algorithms based on their histological and clinical differences.

The Updated International Clinical Recommendations on Scar Management (UICRSM) maintains the effectiveness of their 2002 grading system for distinguishing different classes of scars [2**]. Immature scars are in the process of remodeling. They appear red and mildly elevated with patients occasionally reporting pain and pruritus. Most
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KEY POINTS

- Characteristics of patients at high risk of abnormal scarring include: previous history of hypertrophic or keloid scars, darker skin pigmentation, and scars that traverse relaxed skin tension lines.
- Patients with high risk of abnormal scarring should strongly consider the use of either silicone-based products (silicone gel or silicone elastomer sheeting) or microporous contact media to have the best potential aesthetic outcome.
- Intrallesional corticosteroids remain the first-line treatment for keloids.
- Patients who develop scars unresponsive to first-line treatments should be considered candidates for adjuvant intrallesional corticosteroid and 5-FU (alone or in combination) and laser treatments.

immature scars mature normally and become lightly colored and flat. However, immature scars may also develop into linear hypertrophic scars, which appear red, raised, and pruritic. They may go through a rapid growth phase lasting 3–6 months prior to stabilizing and regressing [2**]. Linear hypertrophic scars can take up to 2 years to fully mature and eventually appear elevated and widened with a rope-like appearance. Widespread hypertrophic scars occur over large areas of the body after burn injuries and also appear red, raised, and itchy. Minor keloids can take up to 1 year after injury to develop and do not spontaneously regress. It is theorized that keloids result from a genetic predisposition to abnormal healing, as recurrence after surgical removal is common. Major keloids appear large and raised over a wide area of normal tissue, rather than focally like the minor keloids [2**].

Silicone gel and elastomer sheeting: properties and mechanism

Many silicone products are available for scar prevention and treatment. Silicone materials are polymers with a silicone–oxygen, or siloxane, backbone chain with additional methyl groups attached through silicone–carbon bonds, generating polydimethylsiloxane units [8]. These are cross-linked to varying degrees to form more adherent but less durable gels (less extensive cross-linking) or less adherent but more durable elastomers (more extensive cross-linking) [9]. Some products have incorporated polytetrafluoroethylene to add durability to low cross-linked silicone elastomer for a product that is both durable and adherent [9].

Silicone gel sheeting (SGS) has been shown to increase hydration of the stratum corneum and decrease evaporation of water from the skin, suggesting hydration and occlusion is the mechanism of action of silicone-based products [10]. Sawada and Sone [11] demonstrated greater improvement in scar quality when an occlusive dressing was combined with silicone cream, than the cream alone.

Related to hydration, increased oxygen permeability is thought to play a role. Hydration of the stratum corneum is thought to increase oxygen...
permeability, thereby reducing hypoxia-induced angiogenesis and tissue growth [12,13].

Temperature change has been hypothesized to improve hypertrophic and keloid scars through increased collagenase activity [14]. A trial of 18 scars treated with SGS demonstrated an increase in skin temperature of 1.7°C compared with adjacent control sites and thought to thereby reduce the amount of collagen in a scar [15].

Direct action of silicone oil on scars has been hypothesized from studies demonstrating silicone in the outer layer of the skin [16,17]. However, the silicone oil products in a study by Branagan et al. [18] were not found in the deeper, viable layers of the skin, and other studies have found no such absorption of silicone products [19,20].

Polarized electric charge created by a silicone cushion has been theorized to shrink scar tissues. A 30-patient study applying silicone oil-filled cushion to hypertrophic scars and keloids demonstrated height and color improvements in two-thirds of the patients within 6 months [21]. The electric action of the silicone oil is thought to be unique to the silicone oil-filled cushions, as increasing humidity under the dressing would dissipate charges in SGS. Although some groups have demonstrated faster cessation of pruritus and flattening of hypertrophic and keloid scars with silicone cushions when compared with silicone sheeting [22], others found no significant difference between the two forms of treatment [23].

**FIGURE 1.** Updated International Clinical Recommendations on Scar Management algorithm for prevention of hypertrophic and keloid scars. (Reproduced with permission from [2**].)

**FIGURE 2.** Photograph of silicone gel sheeting used for scar prevention by 23 h a day application to the forehead scar for 6 weeks after a paramedian forehead flap surgery.
Hypoallergenic microporous paper tape: properties and mechanism

Microporous paper tape is inflexible, microporous, and semiocclusive. Therefore, it is able to reduce tension by supporting the scar, reduce dehydration by mimicking the stratum corneum, and promote healing without bacterial growth seen with other dressings [5]. The tape costs less than $1 for a 10-yard roll and can be worn for up to a week at a time without restriction, making it a convenient and cost-efficient solution.

Using paper tape to reduce tension is based on evidence that there are higher incidences of abnormal wound healing across areas of greater skin tension, such as scars that span Langer's skin tension lines [5]. If tension overcomes initial collagen bonds prior to the scar achieving its maximum tensile strength, there is prolongation of the inflammatory phase, increased fibroblast activity, and increased collagen deposition in haphazard fashion, resulting in hypertrophic scars [5,24].

Hydration is another key mechanism of paper tape. The production of fibroblasts, collagen, and glycosaminoglycan are all reduced in well hydrated tissues [25]. Paper tape is thought to mimic the stratum corneum and reduce evaporative losses from the wound, thereby reducing the risk of abnormal scar formation.

MANAGEMENT

The treatments for hypertrophic scars and keloids are listed in the order of their effectiveness based on the UICRSM (Figs. 3 and 4) [2**].

Hypertrophic scars

Silicone-based therapies

The primary option for the management of hypertrophic scars is silicone-based therapy, either in the form of SGS or a semiliquid silicone gel (SSG). The clinical recommendations suggest a 2-month course of at least 12 h (ideally 24 h) of use per day [2**]. The support for silicone-based products as an initial treatment option includes its availability, cost-effectiveness, and low side-effect profile [26].

Several groups have compared the efficacy of SGS and SSG in scar management. Chernoff and colleagues [4] showed that Dermatix silicone gel treatment resulted in better scar leveling, greater and earlier dissipation of erythema, and superior ease of use compared with silicone sheets in a group of hypertrophic and keloid scars. In contrast, Karagoz and colleagues [27] found no difference between SGS and SGG in their group of postburn hypertrophic scars. The limiting factor for scar improvement with silicone-based therapies is patient compliance [28], and therefore SSG is preferred over SGS in a subset of scars as mentioned in the Prevention section.

Corticosteroid injections

Intralesional steroid injections have historically been the preferred treatment for hypertrophic scars and keloids [29*]. However, recent clinical management studies support the use of corticosteroid injections as a second-line therapy to silicone-based treatments. The UICRSM recommends intralesional corticosteroids as an adjuvant to silicone treatments if a scar fails to improve after 2 months of the silicone gel treatments or when the scar is severe or pruritic [2**]. Triamcinolone is a frequently used intralesional steroid. Triamcinolone injections improve scars via inhibition of fibroblast proliferation, decreased collagen synthesis, and inhibition of collagenase inhibitors [30]. Although the side-effects of triamcinolone are well documented, including skin atrophy, telangiectasia, and hypopigmentation, lower doses of steroids may reduce these effects [6**]. Intralesional corticosteroids can have improved efficacy when combined with other therapies, including 5-fluorouracil (5-FU) and pulse dye lasers (PDLs) [31–33].

Laser therapy

Laser therapy is an adjunct treatment that comes after silicone and intralesional corticosteroids for hypertrophic scars in the UICRSM algorithm (Fig. 3). PDLs with 585-nm lasers are the preferred treatment for both hypertrophic scars and keloids, with emerging evidence favoring ablative and nonablative fractional lasers [6**].

A meta-analysis of scar treatments demonstrated an average 72% rate of improvement or no recurrence with PDL treatment among studies including both hypertrophic scars and keloids [34]. Another systematic analysis demonstrates most evidence of PDL, with less evidence for other laser types, including fractional nonablative laser 1540 nm, CO2 laser 10 600 nm, low-level laser therapy, neodymium-doped yttrium aluminium garnet laser 532 nm, and erbium:YAG laser 2940 nm [35].

There are emerging studies that suggest that ablative fractional laser may be better than PDL for postsurgical scars [36,37]. A histologic study demonstrated that hypertrophic scars and keloids treated with fractional CO2 laser had improved Vancouver scar scores, thinner and more organized collagen, and increased matrix metalloproteinase 9 levels [38*]. However, a recent randomized controlled pilot study has not shown any improvement [39].
**5-Fluorouracil**

5-FU was first reported as a well tolerated and effective treatment for abnormal scarring in 1999 by Fitzpatrick [40]. The UICRSM also notes that 5-FU may be used as an effective second-line treatment for hypertrophic scars unresponsive to silicone-based therapies alongside steroid injections [2**]. Although its benefits are similar to those of intralesional triamcinolone, it has fewer side-effects [29**]. 5-FU tattooing has been proven more effective than intralesional corticosteroids alone [41]; however, 5-FU injections were most effective in scar reduction when used in combined therapies with intralesional corticosteroids and PDL treatments, based on multiple RCTs [31,33]. Finally, the use of 5-FU alone or in combination therapies is contraindicated by pregnancy, anemia, leukopenia, thrombocytopenia, bone marrow suppression, and infection [2**,29**].

**Pressure therapy**

Pressure therapy remains part of the standard of care for widespread hypertrophic scars based on empiric rather than scientific evidence [10]. However, the care of widespread hypertrophic scars remains outside the scope of this study, and therefore only the effectiveness of pressure therapy on linear hypertrophic scars will be considered. A meta-analysis of pressure therapy for treating burn scars found that pressure therapy alone did not improve global scar scores and showed little improvement in scar height [42]. The UICRSM concludes that pressure therapy may have a place in moderate to severe scarring under high pressures [43–45], but is not often effective alone and remains secondary treatment option for more severe scars [2**].
**Onion extract**

Although some studies find that onion extract preparations improve scar qualities and patient symptoms [46,47], an RCT split-scar study showed no difference between it and the standard petrolatum emollient therapy [48]. In addition, onion extract was not found to be as effective as silicone-based products in a comparative study, although this study was treating burn hypertrophic scars rather than traumatic or surgical scarring [27].

**Scar revision**

The UICRSM recommend scar revision after 12 months of conservative treatment without improvement or decreased joint mobility from contracture [2**]. Any tension reducing surgical technique is appropriate and the combination of surgery with adjuvant therapies (e.g., intralesional corticosteroids or 5-FU) to avoid recurrence [2**]. A study by Davison et al. [33] examining the efficacy of 5-FU and triamcinolone found the greatest reduction in scar size from combination of the two therapies with surgical excisions at an average of 92%.

**Keloids**

**Silicone-based therapies**

The UICRSM recommends the use of silicone-based treatment with intralesional corticosteroids for 2–3 months [2**]. A variety of studies have demonstrated the effectiveness of silicone-based products in hypertrophic scars [1]; however, keloid scars are not often studied as a separate scar type [9,23]. One study demonstrated that 75% of patients with keloid scars demonstrated improvement with SGS [49].

**Corticosteroid injections**

Corticosteroids remain a strong, first-line treatment option for both minor and major keloids [2**]. A multitude of studies have demonstrated the efficacy of intralesional corticosteroids with keloids. Many studies combine outcomes of hypertrophic scars and keloids together, with reported rates of response to intralesional corticosteroid injections varying from 50 to 100%. Recently, a study has also demonstrated efficacy in children, finding 82.7% size reduction of keloid scars in pediatric patients [50].

**5-Fluorouracil**

5-FU is recommended for use for both minor and major keloids if there is inadequate response with intralesional corticosteroids alone. The UICRSM considers 5-FU combined with intralesional corticosteroid injections to be the most efficacious treatment after 2–3 months of treatment without improvement in minor keloids and 3–4 months of no improvement in major keloids [2**]. One study found a greater than 50% improvement of keloids in a majority of patients with no recurrence after 6 months and 19% rate of recurrence after 1 year [51]. Generally, 50–70% of scars respond positively to 5-FU treatments [34,52].

**Laser therapy**

The UICRSM recommends addition of laser therapy to scars that fail to improve with just 5-FU/steroids injections after 2–3 months [2**]. Although there are currently limited data, some advisory members on the panel recommend the use of ablative fractional CO2 lasers over PDL [2**]. There have been recent data suggesting positive outcomes with the use of CO2 ablative fractional laser [53–55].

**Scar revision**

Surgical removal remains the last resort for the treatment of refractory keloids and should be avoided in children because of high risk of recurrence [10]. However, the risk of recurrence after surgery remains high, even with adjuvant radiation, but is much lower in craniofacial locations [56]. Postsurgical adjuvant treatments are recommended and include silicone-based therapies, intralesional corticosteroids, and 5-FU. The evidence for success of postexcision 5-FU is the strongest [2**]. Radiotherapy remains a viable, less conservative option to reduce postsurgical recurrence [34,57].

**CONCLUSION**

Based on recent evidence and clinical recommendations, silicone-based therapies are the best option for the prevention and initial management of abnormal scarring. For unresponsive lesions, there are a large number of more invasive options that may be most efficacious in combination therapy, including intralesional injections, laser therapy, and surgical excision. There still remains a scarcity of level 1 evidence surrounding scar management.

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**Conflicts of interest**

There are no conflicts of interest.
REFERENCES AND RECOMMENDED READING

Pages of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- **of outstanding interest**


The article provides an algorithm for the prevention and treatment of scars generated from a review of the literature by the International Advisory on Scar Management.


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