BACKGROUND There is an ongoing need to standardize scar management by establishing safe and effective treatment options that can be applied in routine clinical practice.

OBJECTIVE To review available data on methods for preventing and treating cutaneous scarring.

MATERIALS AND METHODS Relevant scientific literature was identified through a comprehensive search of the MEDLINE database. Additional data and published studies were submitted for consideration by members of the International Advisory Panel on Scar Management.

RESULTS One of the most significant advances in scar management over the past 10 years has been the broader application of laser therapy, resulting in a shift in status from an emerging technology to the forefront of treatment. Accumulated clinical evidence also supports a greater role for 5-fluourouracil in the treatment of hypertrophic scars and keloids, particularly in combination with intralesional corticosteroids. Encouraging data have been reported for newer therapies, including bleomycin, onion extract containing preparations, imiquimod, and mitomycin C, although methodologic limitations in available studies merit consideration. In general, clinical and aesthetic outcomes seem to be enhanced by a combination approach to treatment.

CONCLUSION Advances in therapeutic options and new study data necessitate a revision of algorithms for the prevention and management of cutaneous scarring.

The authors received honoraria from Enaltus, Lumenis, and Merz for their work on this panel.

Prevention and treatment of cutaneous scarring has traditionally lain outside the bounds of standardization; individual experience has been the driver of clinical practice for many years, with varying degrees of success. The 2002 consensus statement from the International Advisory Panel on Scar Management was an effort to ground treatment practices in a foundation of clinical data. Members of the advisory panel reviewed the scientific literature to assess available evidence and shortcomings therein. In the interval since the consensus statement was published, a plethora of clinical trial data have been released, new agents have been tested, and technological advances have enhanced certain existing modalities. In 2012, the advisory panel reconvened to reevaluate support for various treatment methods and ensure that current practices are aligned with the evidence base. The resulting comprehensive literature review update is presented herein. In the interest of brevity, this article focuses on clinical data that have influenced the advisory panel’s recommendations.
Comprehensive Literature Review

A methodology similar to that described in the 2002 publication was used to maintain consistency and allow cumulative evidence to guide this update. A MEDLINE search was conducted to identify relevant clinical trials, randomized controlled trials, comparative studies, and meta-analyses published in English from January 1, 2002, through August 3, 2012. Search terms included avotermin, bleomycin, botulinum toxin, cryotherapy, fluorouracil, hypertrophic, imiquimod, interferon, intralesional, keloid, laser therapy, mitomycin, onion extract, pressure therapy, radiotherapy, scar, silicone, steroid, and transforming growth factor beta 3. In addition, English language review articles discussing the management of hypertrophic and keloid scarring indexed by MEDLINE were assessed, and a manual search was conducted. We confirmed that pertinent literature was included and provided additional review articles, clinical studies, and recent unpublished data for consideration.

Treatment Modalities

Available therapeutic options for the management of cutaneous scarring and the supporting evidence base are outlined in the table below, in order of effectiveness.

- **Silicone-based products**
  - Well established in the management of cutaneous scarring
  - Continues to be widely used in clinical practice
  - Studies deemed susceptible to bias in Cochrane review
  - Newer gel preparations overcome limitations inherent in gel sheeting; appropriate for face and neck
  - Efficacious in scarring prophylaxis and management of hypertrophic scars
  - Silicone gel performed as well or better than silicone gel sheeting
  - Place in therapy largely unchanged over the last decade
  - Preferred first-line treatment for keloids

- **Intralesional corticosteroids**
  - Second-line choice for hypertrophic scars
  - May be combined with other treatments to enhance efficacy
  - Low doses may help minimize side effects, including dermal atrophy, telangiectasia, and hypopigmentation
  - Associated with low rate of keloid recurrence after surgical removal when combined with corticosteroid ointment
  - Successfully used since 1989 for the treatment of cutaneous scars
  - Response rate: 50%–70%
  - Provided same clinical benefit as pulsed-dye laser therapy or intralesional triamcinolone, with fewer side effects
  - 5-FU tattooing provided more significant improvement versus intralesional triamcinolone
  - Addition to scar reduction therapies enhanced therapeutic efficacy versus each treatment alone
  - 5-FU + intralesional triamcinolone versus triamcinolone
  - 5-FU + intralesional triamcinolone versus surgical excision and triamcinolone
  - 5-FU + pulsed-dye laser therapy + triamcinolone, versus triamcinolone
  - 5-FU + intralesional corticosteroids reduced recurrence rate after surgical removal of ear keloids
  - Considered an emerging technology in 2002 guidelines
  - Pulsed-dye laser therapy first to gain widespread acceptance
  - 585-nm pulsed-dye laser preferred choice for both hypertrophic scars and keloids

- **5-Fluorouracil**
  - Successfully used since 1989 for the treatment of cutaneous scars
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- **Laser therapy**
  - Considered an emerging technology in 2002 guidelines
  - Pulsed-dye laser therapy first to gain widespread acceptance
  - 585-nm pulsed-dye laser preferred choice for both hypertrophic scars and keloids

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Estimated 72% efficacy rate\textsuperscript{12}

- Greater efficacy thought possible with 595-nm pulsed-dye laser\textsuperscript{25}

- Significant improvement after only 2 sessions\textsuperscript{24}

- Addition of intral esional corticosteroids has little impact on outcomes, except in highly symptomatic cases\textsuperscript{26}

- Ablative and nonablative fractional lasers are focus of much current research

- Generally favorable in scientific literature for preventative and treatment applications\textsuperscript{27-36}

- Better outcomes with fractional versus pulsed-dye laser in postoperative treatment of surgical scars\textsuperscript{29,32}

- Improvements in clinical and structural features of burn scars reported with fractional CO\textsubscript{2} laser therapy\textsuperscript{33-35}

- Ablative fractional lasers require fewer sessions, thus may be preferred over nonablative lasers for burn scars\textsuperscript{35}

- Common side effects after fractional laser treatment: transient erythema, edema, and purpura\textsuperscript{27,28,30}

- Ablative fractional laser + triamcinolone acetonide may provide an efficient, safe, and effective therapy for challenging cutaneous scars\textsuperscript{37}

- Common side effects after fractional laser treatment: transient erythema, edema, and purpura\textsuperscript{27,28,30}

- Ablative fractional laser + triamcinolone acetonide may provide an efficient, safe, and effective therapy for challenging cutaneous scars\textsuperscript{37}

- Radiotherapy

- Continues to be reserved for secondary management in adults with cutaneous scarring

- Combined with surgical excision, radiotherapy

- Decreased keloid recurrence rates\textsuperscript{12,13}

- Produced fewer side effects and greater patient satisfaction than cryotherapy and intral esional corticosteroids\textsuperscript{38}

- Reduced recurrence rates when treatment tailored to body region\textsuperscript{39}

- Recurrence also prevented with high-dose-rate superficial brachytherapy after keloidectomy\textsuperscript{40}

- Historically limited to small scars because of\textsuperscript{1}

- Need for repeated treatments

- Prolonged healing times

- Potential for permanent pigmentation alterations

- Skin atrophy

- Pain

- Intral esional rather than contact cryotherapy substantially reduced cutaneous scar volume during one treatment, with minimal side effects and rapid recovery\textsuperscript{41,42}

- Improvements in scar hardness, elevation, redness, itching, pain, and tenderness also reported; no evidence of permanent hypopigmentation\textsuperscript{43}

- Intral esional versus contact cryotherapy was less painful during and immediately after treatment\textsuperscript{44}

- Traditional cryotherapy combined with intral esional corticosteroids augments therapeutic efficacy in small keloids\textsuperscript{45}

- Eases corticosteroid injection through creation of an edema in the dermis, thereby increasing efficacy\textsuperscript{41,45}

- Bleomycin

- Efficacy in treatment of cutaneous scarring demonstrated in multiple small and uncontrolled studies\textsuperscript{46}

- Most patients experienced substantial scar flattening or regression, amelioration of pain and pruritus\textsuperscript{47,48}
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<tr>
<th>Treatment</th>
<th>Summary</th>
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<td>Mitomycin C</td>
<td>- More favorable therapeutic response versus cryotherapy + intralesional triamcinolone demonstrated in only 1 study⁴⁹</td>
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<td></td>
<td>- No keloid recurrence after 6–24 months with surgical excision and topical mitomycin C⁵⁰</td>
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<td>- Keloid worsening and ulceration reported with intralesional mitomycin C⁵¹</td>
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<td></td>
<td>- No improvement in keloid recurrence rates reported in only 1 study⁵²</td>
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<td>- Mostly small and uncontrolled studies, with high degree of methodologic variability⁵³</td>
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<td>- Little available data for hypertrophic scarring; mostly clinical experience in postoperative management</td>
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<td>Imiquimod</td>
<td>- 5% cream effective in prevention of earlobe keloid recurrence after excision⁴⁶,⁵³,⁵⁴</td>
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<td>- However, high rate of recurrence reported for trunk keloids after excision and 8-week imiquimod treatment⁵⁵</td>
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<td>- Recurrence rate also substantially different between lesions of the pinna and chest wall or neck⁵⁶</td>
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<td>Pressure therapy</td>
<td>- Longtime standard care for prevention and treatment of hypertrophic scars from burns, practice largely based on empiric evidence¹</td>
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<td>- No change in global scar scores and only small improvement in scar height reported in meta-analysis⁵⁷</td>
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<td>- Low pressure less effective than high-pressure treatments; patients with moderate or severe scarring experienced greater clinical benefit⁵⁸–⁶⁰</td>
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<td>Adhesive microporous hypoallergenic paper tape</td>
<td>- Recommended in 2002 guidelines for prevention of hypertrophic scarring after surgical incision in low-risk patients¹ on the basis of advisory board consensus rather than controlled clinical trial data</td>
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<td>- Significant improvements versus placebo in cosmesis, induration, pigmentation, and tenderness of cutaneous scars reported in prospective study⁷⁰</td>
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**Generally well tolerated, alone or in combination**
Emerging and Investigational Therapies

Reduction of muscular tensile force during scar formation and restoration of balance between fibroblast proliferation and apoptosis may represent a novel therapeutic option for the aesthetic improvement of postsurgical scars. Botulinum toxin A (BTA) paralyzes local muscles and reduces skin tension caused by muscle pull, thereby decreasing scar tension and subsequent inflammation in wound edges. Gassner and colleagues demonstrated that BTA injections resulted in enhanced wound healing and less noticeable scars compared with placebo. Recently, intralesional injection with BTA was also proposed for the treatment of established keloids. In a prospective uncontrolled study, BTA was injected into lesions at 3-month intervals for a maximum of 9 months. At 1-year follow-up, scar regression was noted from the periphery in all 12 patients, followed by flattening of lesions; no signs of recurrence were noted in any patient. However, in a recently published study, objective evaluation of BTA-treated keloids using optical profilometry did not reveal any changes after BTA therapy compared with baseline. Thus, although reduction of the tensile force by prophylactic BTA injections might represent a comprehensible mechanism of action for aesthetic improvement of postsurgical scars, the suggested clinical efficacy of intralesional BTA for the treatment of existent keloids remains uncertain. More in-depth studies are needed before a comparatively expensive therapy can be suggested for this particular indication.

A novel hydrogel scaffold product was recently approved in Europe for the improvement of wound healing and resulting scars. Unpublished data from a randomized controlled trial revealed improvement in surgical scar ratings after a single application. When used in the treatment of earlobe keloids, preliminary results indicated a significant reduction in 12-month recurrence rate after a single injection after surgical excision compared with historical data.

Other innovative therapies that have been evaluated for the prevention and management of scarring (e.g., calcineurin inhibitors, retinoic acid, tamoxifen, verapamil) have insufficient evidence for recommendation in routine clinical practice. It is worth noting that avotermin, a human recombinant transforming growth factor beta-3 derivative, showed promising results in preclinical and early clinical development as a prophylactic treatment for scarring yet failed to meet the primary or secondary end points in the Phase 3 REVISE trial. Another agent with early potential, interferon α2b, has yet to clearly establish a role in the prevention and management of pathologic scarring. Accumulated evidence for interferon α2b is mixed, with some studies demonstrating a positive impact on prevention of keloid recurrence and reduction of scar size and others showing no such benefit. Side effects, such as flu-like symptoms and pain at the injection site, as well as the expense of treatment limit the applicability of interferon therapy.

Conclusion

Clinicians have a host of therapeutic options for the management of cutaneous scarring at their disposal. Despite a persistent gap in the scientific literature needed to support many of the procedures routinely applied, evaluation of the clinical evidence revealed appropriate scenarios wherein use of a particular therapy or combination of therapies is efficacious in improving scars. To promote application of treatment modalities consistent with the current evidence base, a revision to scar prevention and treatment algorithms is necessary.

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References


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