Treatment of Scars: A Review

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Hypertrophic Scars and Keloids

The complex interplay of events that occurs following injury to the skin does not always eventuate in a normal, smooth skin surface. Rather, the skin often responds to injury with a proliferation of fibrous tissue. When tissue response to injury is overzealous, the result is a hypertrophic scar or keloid.

By definition, hypertrophic scars remain within the boundaries of the original wound, whereas keloids extend beyond the original area of skin injury (Figs 1 and 2). Some authors include a temporal component to differentiate these two types of lesions as well, suggesting that a hypertrophic scar that is present for greater than 12 months and with margins that extend beyond the original site of the wound evolves into a keloid [1]. The time between cutaneous injury and the onset of hypertrophic scar or keloid formation may vary from weeks to years, but hypertrophic scars differ from keloids in their tendency to regress spontaneously over time, while keloids remain elevated [2]. Despite these definitions, hypertrophic scars and keloids are difficult to differentiate in many circumstances due to the fact that their clinical characteristics often overlap.

Histologically, keloids and hypertrophic scars are composed of thick, hyalinized collagen bundles arranged in nodules consisting of small fibrocytes and separated by bands of immature fibroblasts [3]. There are multiple microvessels that often appear occluded by an excess of endothelial cells [4]. Keloids have additionally been shown to contain an increased amount of hyaluronidase.

Many different theories have been proposed to explain the array of clinical presentations of scars. Complex biological systems, including biochemical, metabolic, and immunological, have been implicated in hypertrophic scar and keloid formation [5–8]. However, because of the interdependence of the steps involved in the wound-healing cascade, it has been impossible to separate the events sufficiently to implicate any one cell type or blood-borne factor as being responsible for keloid and hypertrophic scar formation.

Wound healing is arbitrarily divided into three phases: inflammation, granulation tissue formation, and matrix remodeling. The first phase, initiated by neutrophils, involves a well-organized cascade of inflammatory cells. Later, macrophages, which may be the most important cells in wound healing, elaborate a variety of cytokines that influence the wound environment and eventuate in granulation tissue formation. Finally, fibroblasts migrate into the area, proliferate, and recapitulate ontogeny by depositing new collagen—first as type III and later as type I. Simultaneously, angiogenic factors released into the wound result in the formation of new capillaries. Under ordinary circumstances, scar maturation occurs due to the regression of stimulatory factors. Coincident with scar maturation is a decrease in angiogenic stimuli and, therefore, a decrease in the hyperemia associated with early wound repair. Collagen synthesis and remodel-

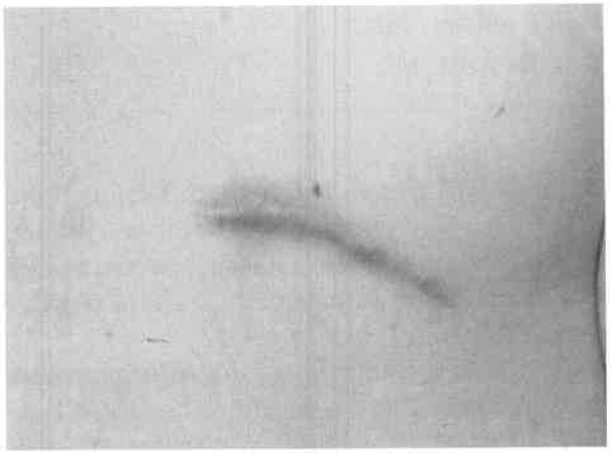


Fig 1. Hypertrophic scar within the borders of the original incision.

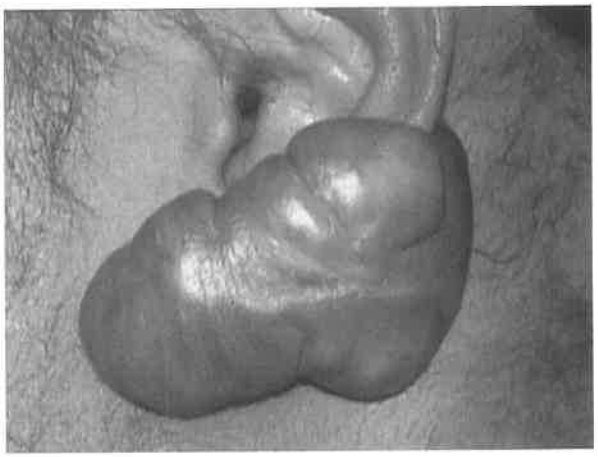


Fig 2. Keloid of the ear, showing extension of the scar beyond the initial ear-piercing wound.

ing also normalize within 6 to 12 months of the initial tissue injury. While scars never regain 100% of their original tensile strength, they eventually achieve approximately 70% to 80% of the strength of normal skin.

Various factors, including ethnic background and location of injury, are thought to be important in determining whether a scar heals in a cosmetically acceptable manner or develops into a keloid or hypertrophic scar. Hypertrophic scars and keloids affect approximately 4.5% to 16% of the black and hispanic population. Caucasians are less susceptible, with a white-to-black susceptibility ratio estimated at 1:3.5 to 1:15 [9]. Keloids result from an inherited metabolic alteration in collagen [10]. Both types of scars occur most commonly on the back, chest, shoulders, and earlobes. Other high-incidence areas include the proximal upper limbs, the pectoral areas, and the lower face [11]. They may arise in areas that have been traumatized (e.g., burns, surgery, acne, vaccinations), but may also occur spontaneously, especially on the anterior aspect of the chest. They are most commonly observed between 10 and 30 years of age [2, 9, 12]. Clinically, hypertrophic scars occur less frequently and are usually milder in severity after sutured surgical incisions than they are after burns or other wounds in which epithelialization is delayed. Scars can also be more severe following poorly designed surgical wound closures (with excess tension placed on the wound) and following wound infection. Hypertrophic scars usually occur within the first 6 to 8 weeks after skin reepithelialization and undergo a rapid growth phase that can last up to 6 months, with gradual "maturation" over the next 1 to 2 years [13]. In some patients they may gradually disappear, while in others they continue to enlarge and may last a lifetime [14]. The excess collagen produced in these abnormal wounds is probably related to oversynthesis rather than to an increase in the absolute number of fibroblasts. The resulting overproduction of collagen surpasses collagen degradation during the remodeling phase of wound healing, resulting in hypertrophy [15]. Investigators have demonstrated decreased expression of collagenase in hypertrophic scar fibroblasts, suggesting a possible etiological mechanism for the excessive accumulation of collagen in hypertrophic scars [16].

The presence of a keloid or hypertrophic scar is frequently cosmetically unacceptable to the affected individual. In addition, it may be painful or pruritic and may restrict range of motion. Physicians have attempted to improve the appearance of scars by both physical and chemical means for many years. Various methods of manipulation have been enlisted to normalize their topography as well as to eliminate erythema and dyspigmentation. Because the treatment of scars is often undertaken for, at least in part, cosmetic concerns, it must be free of adverse sequelae in addition to being effective.

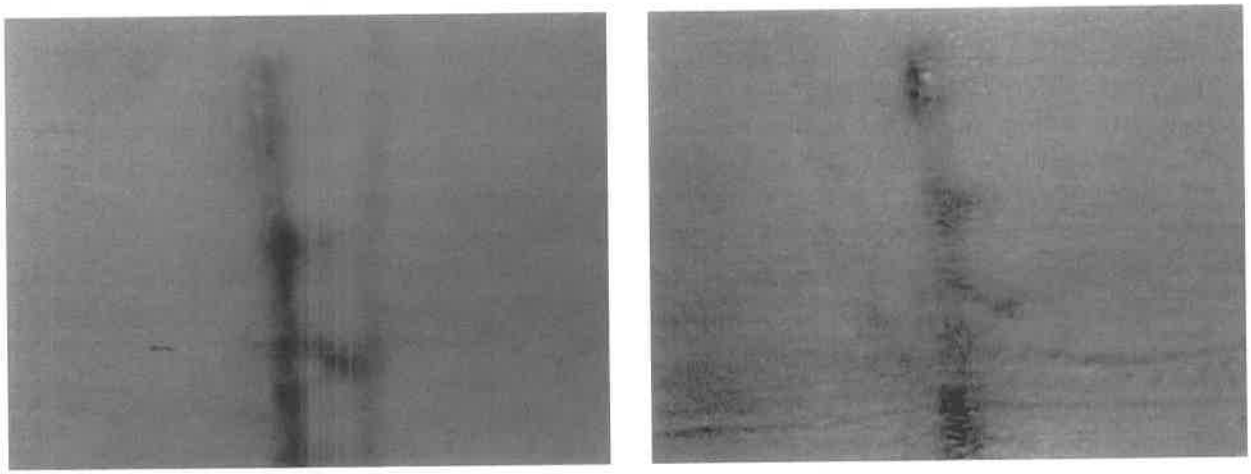
There is no universally accepted treatment modality resulting in permanent hypertrophic or

keloid scar ablation. Surgical excision is usually followed by recurrence unless concomitant prophylactic measures are employed, because the new surgical wound is prone to the same mechanical, immunological, and biochemical forces as the original scar. Recurrence rates following excisional surgery alone have been estimated at 45% to 100% [17].

Proposed management or prevention of scars include three distinctly different therapeutic approaches: (1) correction of abnormal collagen metabolism when the equilibrium between collagen synthesis and degradation has been destroyed, (2) alteration of the immune/inflammatory response, and (3) manipulation of the mechanical properties of wound repair [18]. Systemic and local pharmacological treatments have been advocated for keloids and hypertrophic scars that take into account these three approaches. Colchicine has been shown to affect collagen metabolism at three points: inhibition of collagen synthesis by disruption of microtubular systems, stimulation of collagenase, and interference with wound contraction by a direct effect on the myofibroblasts [15, 19]. Antihistamines have been instituted in the treatment of hypertrophic scars based on the observation that mast cells may play a role in scar formation [20]. Lathyrogens, such as D penicillamine and beta aminopropionitrile, prevent collagen cross-linking after its secretion from the fibroblast, increasing its vulnerability to enzymatic degradation. Local methods of manipulation have included topical and intralesional steroids [21, 22], topical application of retinoic acid [23, 24], intralesional hyaluronidase [25], topical zinc [26], topical vitamin E [27], topical putrescine to modify type III collagen cross-linking [28], surgical revision [29], radiation therapy [30, 31], pressure therapy [32], silicone gel sheeting [10, 33–37], cryotherapy [38–40], and laser treatment [41–60]. Most of these treatments are associated with high recurrence rates and several may lead to significant side effects or be painful or inconvenient, resulting in decreased patient compliance.

Intralesional injection of corticosteroid has been a cornerstone of both treatment and prophylaxis of hypertrophic scars and keloids [21, 61–63]. When surgery is combined with intradermal corticosteroids the recurrence rate in the majority of studies falls below 50% [17]. The effect of corticosteroids may be explained in part by interruption of the inflammatory response [1]. The specific mechanism of action of corticosteroids is related to both suppression of collagen synthesis and to the release of collagenase inhibition resulting in collagen catabolism. Once considered the standard treatment for hypertrophic sternal scars [63], intralesional injection with triamcinolone solution has shown clinical efficacy but has also been associated with multiple side effects including atrophy, white beadlike skin deposits, pain on injection, and pigmentary changes in up to 63% of patients [64]. In addition, intralesional corticosteroid injection may result in the development of telangiectasias overlying the treated area.

The molecular basis for the excessive fibrosis that results in the formation of keloids and hypertrophic scars has not been delineated. However, investigators have begun to study the role of products of the inflammatory response and the regulation of collagen synthesis in scar formation. Interleukin-1, produced by monocytes, increases collagen and fibronectin synthesis by fibroblasts. In contrast, recombinant human interferon gamma has been shown to downregulate collagen synthesis and may be useful in the treatment of diseases characterized by collagen overproduction [65]. Based on data from Kahan and colleagues, who used recombinant human interferon gamma to treat 10 patients with systemic sclerosis [66], Larrabee and associates used this lymphokine to treat 10 patients with hypertrophic scars and keloids. Larrabee et al reported moderate clinical and symptomatic improvement in patients with existing abnormal scars, however the most dramatic result was achieved in a patient who was successfully prophylaxed with interferon gamma following keloid excision. Side effects, including headache, reversible granulocytopenia, and elevation of hepatic transaminase levels, are dose- and route-dependent [1]. The probable mechanism of action of interferon gamma in downregulating collagen is through reduction in cellular messenger ribonucleic acid (mRNA) [67, 68]. In contrast to steroids, which produce a general reduction in the inflammatory response, recombinant human interferon gamma targets a specific site of action in the fibroblast



A B

Fig 3. (A, B) Hypertrophic scar on the abdomen (A) before and (B) after 6 months of nightly silicone gel sheeting.

that reduces collagen production. Whether there is an excess of interleukin-1 or a deficiency in interferon gamma in individuals with a tendency to develop abnormal scars has not been determined.

Growth factors known to modulate wound healing include basic fibroblastic growth factor, the BB isoform of platelet-derived growth factor, insulinlike growth factor-I (IGF-I) and transforming growth factor beta (TGF-β) [69]. Recently it has been suggested that IGF-I-induced suppression of collagenase mRNA and activity may be a mechanism by which IGF-I promotes the development of postburn hypertrophic scars [69]. TGF-β is released by platelets at the site of injury and is highly chemotactic for macrophages and monocytes. It also stimulates production of collagen and fibronectin by fibroblasts, probably by enhancing the effect of epidermal growth factor on the fibroblastic population, stimulating epithelial differentiation and initiating deoxyribonucleic acid (DNA) and RNA synthesis [71–73]. Roberts and colleagues have suggested that excess production or abnormal sensitivity to this ubiquitous growth factor may be important in pathologic fibrosis, not only in wounds but also in other systemic fibrotic disorders [74].

Since the first report by Perkins and associates [73] in 1982, various investigators have demonstrated significant scar improvement following application of topical silicone gel sheeting for 2 to 4 months [10, 13, 34, 74–78] (Fig 3). Topical application of silicone gel to scars for at least 12 hours daily has been shown not only to provide early relief of symptoms and to enhance patient compliance due to the lack of pain associated with the treatment [64], but may also prevent hypertrophic and keloid scar formation [79]. Katz [78] demonstrated that 79% of scars treated immediately after reepithelialization (following full-thickness surgical revision and scar abrasion) with silicone sheeting did not recur within 6 months.

The effect of silicone gel has been shown to be unrelated to pressure [75], but may depend on scar hydration instead [35–37]. Recent studies using occlusive silicone creams have confirmed that silicone gel sheets function through scar hydration and occlusion [35–37, 80]. Phillips and colleagues [80] demonstrated a significant reduction in pruritus and pain, and an increased pliability within hypertrophic scars, but not keloids, treated with hydrocolloid dressing or moisturizer for 2 months. Scar pigmentation and elevation, however, remained unchanged [81]. While the mechanism by which hydration exerts its effects on scars is unknown, the reduction in water vapor loss is postulated to decrease capillary activity, thereby reducing collagen deposition and scar hypertrophy [82]. Wood and coworkers [83] have reported that occlusion decreases interleukin-1α mRNA. Interleukin-1 is a proinflammatory cytokine exhibiting pleiotropic effects that include a direct increase in fibroblastic collagenase glycosaminoglycan synthesis. This cytokine also increases the production of interleukin-6,

which in turn activates human fibroblastic synthesis of extracellular matrix components [84]. It has yet to be determined whether silicone-based or nonsilicone-based sheeting is more effective in the treatment of scars.

A continuous pressure of approximately 80 mmHg has been shown to elongate and flatten some scars due to remodeling of scar collagen [84]. The mechanism through which continuous pressure reduces the size and thickness of keloids and hypertrophic scars is unknown, but may be related to a demonstrated reduction of intralesional mast cell numbers and consequent reduction in histamine production [86]. Local tissue hypoxia has also been proposed as the mode of action through which continuous pressure exerts its effects, as compressed keloids have significantly reduced tissue oxygen (pO_2) levels and increased tissue carbon dioxide (pCO_2) levels when compared with normal tissue [87].

Physical manipulation of keloids and hypertrophic scars has been attempted with the use of cryotherapy. The therapeutic effects of cryotherapy are related to direct cell damage as well as to changes in the microcirculation initiated by freezing, which leads to stasis of blood and subsequent dermal anoxia. Finally, occlusion of vessel lumina with thrombi produces tissue necrosis and sloughing. The collagen fibers that subsequently form are flat and normal in quantity, with axes parallel to the skin surface [40]. Treatment usually involves two or three freeze-thaw cycles at each of the 2 to 10 treatment sessions. Layton and Colleagues [38] reported that cryosurgery was more effective than intralesional triamcinolone in the treatment of acne keloids. Keloids on the face, as well as those that were grossly palpable, however, showed a poor response to both treatment modalities. Those keloids that demonstrated greater blood flow by Doppler, and that were also more clinically erythematous and of more recent onset, responded better to both treatments compared with less vascular lesions. This study was flawed by its short follow-up of only 8 weeks as well as its limitation of each treatment to two sessions. Zouboulis and coworkers [39] in their randomized prospective study of 93 white patients with keloids and hypertrophic scars, found improved responses in those patients treated with three or more sessions compared with individuals treated once or twice. They reported excellent responses in 32.3%, good responses in 29%, and no response in 9.7%. Responders exhibited no progressions or recurrences in an average follow-up period of 32 months [39]. These results may be biased in terms of their applicability to keloids and hypertrophic scars in general because the authors excluded individuals with darker skin tones who are known to demonstrate a higher recurrence rate. Several authors have reported that cryotherapy offers no better results than simple surgical excision [3, 88]. Rusciani and associates [40] suggest that the reported lack of efficacy may be due to inadequate freeze times or the failure to continue treatment when the results of the initial freeze are less than outstanding. In their series, complete flattening was achieved in 73% of 65 scars and there were no recurrences at an average follow-up of 31 months. Side effects were limited to hypopigmentation and light to moderate atrophy in 3 patients. The hypopigmentation due to the cold sensitivity of melanocytes is largely permanent and renders cryotherapy less desirable in dark-skinned patients. The postoperative phase may be disturbing to the patient because cryotherapy produces an open wound that takes several weeks to heal [40]. Better results may be achieved with active keloids of less than a 2-year duration because collagen synthesis and degradation is typically normalized to levels similar to those of normal scars beyond that time [89]. In addition, pedunculated lesions are thought to respond better than those on a broad base due to the more limited vascular supply of the former [40].

Excision followed by radiation therapy has been touted as a useful and effective method of keloid eradication [31, 90–94]. The effectiveness of radiation therapy is thought to relate to its inhibition of neovascular buds and proliferating young fibroblasts associated with early wound healing, resulting in a decreased amount of collagen production [95]. Klumpar and coworkers [96] found that the electron beam offers no advantage over orthovoltage radiation after comparing the two modalities in the treatment of 186 patients over 17 years. Doornbos and associates [90] analyzed a large series of patients treated over a 25-year period and concluded that the total radiation dose is more significant than the timing of

treatment initiation, the size of the fraction given, the duration of treatment, or the location of the keloid. The authors recommended a dose of at least 1,500 cGy [90]. Radiation therapy has traditionally been associated with the development of side effects such as local hypo- and hyperpigmentation, erythema, telangiectasia, and atrophy. Recently, Sclafani and colleagues [30] reported only a 12.5% incidence of earlobe keloid recurrence when radiation was used as an adjunct to excision, while adjunctive steroid injection resulted in a recurrence rate of 33%. While these authors noted no alteration of skin pigmentation, wound dehiscence, chronic dermatitis, or neoplastic change, controversy continues over whether to treat benign lesions with radiation therapy due to the perceived risk of adverse long-term sequelae. It has been suggested that radiation is not practical for use in children or in areas of potential carcinogenesis including the breast and thyroid gland [1, 12]. However, only two cases of malignancy have been reported in patients who underwent excision followed by radiation therapy and both tumors were thought to be unrelated to the treatment [97]. Radiotherapy may also be used in the treatment of established keloids, although recurrence rates are higher than when radiation is delivered after excision [31, 90].

Bailin [98] first reported good results in a series of patients with keloids excised by the continuous-wave CO_2 laser in 1982. The laser's beneficial effect was attributed to its nontraumatic and anti-inflammatory properties [98]. In 1991 Norris [58] further evaluated the efficacy of CO_2 laser excision as a primary modality for the treatment of keloids. Of 31 patients retrospectively studied, only 1 subject was free of recurrence while 9 other patients required intralesional steroids to suppress recurrence and 13 others were judged to be treatment failures [58]. It was concluded that CO_2 laser excision of keloids fails to suppress their growth and recurrence. This conclusion was later corroborated by Apfelberg and associates [54] in 1989 when 7 patients with nine keloids, located on the trunk, nuchal region, back, and earlobe, were treated by CO_2 laser excision. Only 1 patient, after earlobe keloid excision, experienced marked improvement, which was maintained for 9 months, but required the continuous use of pressure earrings [54]. Following their experience treating a patient with a large truncal keloid, Olbricht and Arndt [99] concluded that CO_2 laser excision of keloids should be reserved for special situations such as large or draining keloids that require debulking before the institution of other measures to control regrowth.

Since 1983 when Anderson and Parrish [100] published their landmark paper describing the theory of selective photothermolysis, laser technology has exploded with the development and refinement of a myriad of high-energy, target-specific pulsed and scanned laser systems. Prior to that time, lasers were less selective and often resulted in nonspecific thermal damage to tissue surrounding the treated area. The newer high-energy pulsed and scanned lasers have revolutionized the treatment of many skin disorders by the precise targeting of specific tissue components resulting in a vast reduction of scarring as a sequela of treatment.

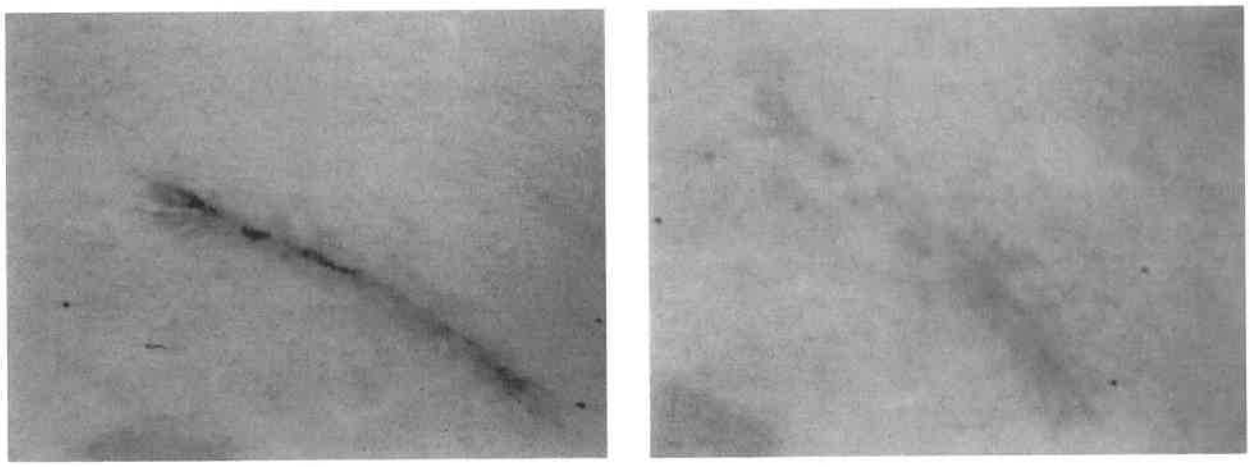
The argon laser was one of the first lasers applied to the treatment of keloids and hypertrophic scars. Ginsbach and Kohnel [101] in 1978 were the first to report encouraging results with the argon laser in the treatment of hypertrophic scars. The argon laser was thought to work by coagulation of the capillary plexus leading to an area of localized anoxia with the production of lactic acid by glycolysis. The resulting decreased pH was believed to lead to granulocytic lysis with the release of enzymes, including collagenase. This increase in tissue levels of collagenase was postulated to be a direct result of laser treatment, but was also thought to be an indirect result of a decrease in $alpha_2$ macroglobulin, a collagenase inhibitor. The resulting increase in collagenase, by either mechanism, would result in increased collagenolysis, which would then lead to the flattening of hypertrophic scars [55, 101]. However, another study in 1984 failed to corroborate the efficacy of the argon laser, with only approximately one half of 82 patients achieving a good to excellent objective response following argon (77 patients) and CO_2 (5 patients) laser treatment. No symptomatic improvement associated with the scars was seen in 80% of treated patients within 14 days postoperatively [55]. Apfelberg and associates [53] divided keloids into thirds for the purpose of comparing argon and CO_2 laser irradiation to control (nontreated) sites in 13

patients with keloids of 5.6 years average duration. While several of the treated patients experienced temporary symptomatic improvement, only one maintained a response at the 6-month follow-up [53]. Hulsbergen-Henning and colleagues [57] showed similar results with only 3 of 45 patients treated with the argon laser demonstrating scar improvement (decreased color and size) of more than 50%. These authors postulated that the mechanism of action of the argon laser was related to heat conduction causing shrinkage of dermal tissue, but that the treatment was superficial, resulting in only temporary scar improvement [57].

The neodymium:yttrium-aluminum-garnet (Nd:YAG) laser (1064 nm, continuous wave) has been shown to exert an effect on collagen metabolism. Initial studies showed decreased collagen content in Nd:YAG laser-treated pig skin [101]. Later, collagen production was shown to be selectively inhibited by a direct photobiological effect of this laser, while DNA replication and cell viability of fibroblasts were unaffected [56]. A follow-up study documented 2 patients, each followed for 3 years, in whom treatment of keloids with the Nd:YAG laser resulted in significant flattening, softening, reduction in size, and normalization of color. The authors postulated that perhaps even more effective keloid eradication could be achieved by a combination of conventional excision or CO_2 laser vaporization of excess tissue followed by Nd:YAG laser treatment to suppress collagen production [56]. The Nd:YAG laser appeared to work by infarction with subsequent charring and sloughing of the irradiated area, which was then left to heal by secondary intention. A deterrent to the use of lasers in the visible or near-infrared spectrum is the presence of large amounts of melanin in the epidermis because laser energy is absorbed by the pigment at a superficial level, resulting in reduced thermal injury to the deeper target tissue. The Nd:YAG, argon, and CO_2 lasers can each temporarily decrease collagen synthesis, thus providing a distinct advantage over scalpel excision, which cannot. Keloids remain a distinct problem, however, as they represent a permanent change in physiology manifested as an inability to regulate a balance between collagen synthesis and lysis in wound healing [59].

Persistent erythema in scars is the result of excess vasculature. Increased vascularization results in fibroblast proliferation and excess collagen accumulation. Over the past 10 years great strides have been made with the use of the 585-nm vascular-specific flashlamp-pumped pulsed dye laser in the treatment of hypertrophic and/or erythematous scars and keloids. However, the exact mechanism whereby hypertrophic and keloid scars are altered by the 585-nm laser system remains unknown. The first study demonstrating an improvement in scars using the 585-nm pulsed dye laser was reported by Alster and colleagues [47] in 1993. Ten argon laser-induced scars within port wine stains received five laser treatments over a 10-month period. Using optical profilometry to measure skin surface texture, the authors demonstrated a return of normal skin markings after 585-nm irradiation, representing a change in the surface texture of the treated scars to more closely resemble that of normal skin. The improvement was manifested either as flattening of the hypertrophic portions of the scars and/or the reappearance of skin surface markings in the scarred areas. This study represented the first use of an objective parameter (optical profilometry) to assess the degree of improvement in scar texture as an adjunct to subjective evaluation by observation and photography. Histological examination demonstrated that the dilated vascular channels present in scar tissue resolved following laser treatment in 8 of 10 patients but remained unaltered in 2 others. The improvement in the laser-treated scars persisted at the 6-month study follow-up examination and Alster [43] later reported that no recurrence or worsening of the scars occurred in the 4 years following treatment.

In a subsequent study of 14 patients with erythematous scars, Alster [41] demonstrated a 57% to 83% improvement with the 585-nm flashlamp pulsed dye laser following one or two treatments respectively (Fig 4). The clinical improvement, which included softening and flattening of the scars as well as decreased erythema, persisted at the 6-month follow-up examination [41]. More recently, Alster and McMeekin [49] showed that hypertrophic facial acne scars demonstrated significant clinical and textural improvement within one to two laser sessions using the 585-nm



A B

Fig 4. (A, B) Hypertrophic scar on the breast (A) before and (B) 6 weeks after a second treatment with a 585-nm pulsed dye laser.

pulsed dye laser. The average energy densities used in these studies ranged from 6.0 to 7.0 J per square centimeter with a 5-mm spot size.

The first controlled study of the response of hypertrophic scars and keloids to the 585-nm flashlamp-pumped pulsed dye laser was performed on median sternotomy scar halves by Alster and Williams [51] in 1995. The authors objectively demonstrated the difference between laser-treated and untreated scar tissue by analyzing skin surface textures, histological specimens, erythema and height measurements, pliability scores, and symptomatology. The significant improvement observed in each of these study parameters within the laser-irradiated scar halves persisted for at least 6 months following treatment.

In an uncontrolled study, Dierickx and associates [52] treated 15 patients with erythematous/hypertrophic scars refractory to various traditional treatment modalities with the 585-nm pulsed dye laser. The authors reported that an average of 1.8 laser treatments at fluences ranging from 6.0 to 7.5 J per square centimeter delivered through a 5-mm spot size produced an average improvement of 77%. Scars less than 1 year old tended to respond more readily to treatment than older scars, as did facial scars in comparison to those on the extremities or buttocks. While the initial objective of the study was to improve the color of the scars, the authors reported subjective softening and flattening as an unexpected consequence of laser therapy [52]. Similar conclusions were reached by Goldman and Fitzpatrick [103], who treated 48 patients presenting with erythematous/hypertrophic scars with the 585-nm pulsed dye laser with or without concomitant intralesional steroids. Patients who received combination treatment with simultaneous administration of intralesional steroids (5 to 10 mg per milliliter) and laser treatment appeared to achieve greater resolution than those treated with the laser alone, although it was unclear from the report exactly which patients received the combination treatment [103].

Initially, the 585-nm pulsed dye laser was directed at the vascular component of scars to reduce or eliminate persistent erythema, with the softening and flattening of the treated scars as an incidental finding. There is no consensus on the mechanism of improvement in scar texture produced by this vascular-specific laser. Some plausible theories include a decrease in cellular nutrition and function within the irradiated scar through the laser's vascular specificity, leading to decreased microvascular perfusion, an alteration of the ratio of collagen metabolism resulting in catabolism as the overriding force by laser-induced tissue hypoxia, superheating of collagen fibers resulting in dissociation of disulfide bonds, and subsequent organized realignment of collagen fibers [52]. Because fibroblastic growth and other factors are known to be affected by histamine, another likely explanation for the effective-

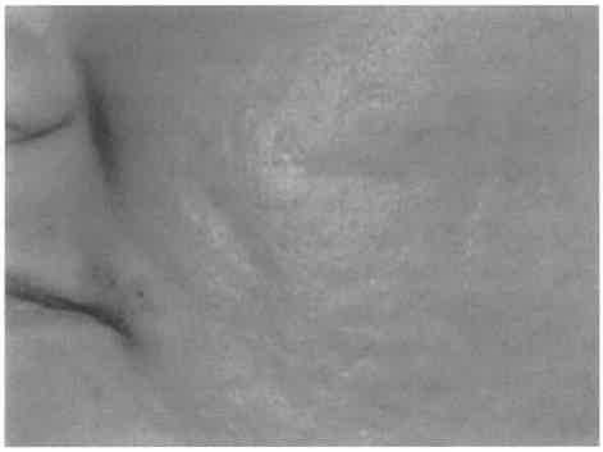


Fig 5. Atrophic acne scars on the face.

ness of the 585-nm laser may be related to the increase in regional mast cell numbers observed after laser irradiation [51].

In terms of patient selection for the treatment of scars with the 585-nm pulsed dye laser, individuals with pale skin phototypes (I or II) are the best candidates because the increased amount of melanin in darker skin competes with hemoglobin for absorption of the laser energy. The most appropriate timing of treatment has not yet been determined. While scars may improve spontaneously during the first 6 to 12 months after integumental injury, especially in terms of erythema, anecdotal evidence suggests that earlier treatment of scars, within the first month following surgery or trauma, may prevent hypertrophy in individuals who are keloid prone [43, 46, 104, 105]. Perhaps the initiation of laser treatment within the first few weeks following injury may prevent or arrest scar proliferation so that fewer laser sessions may be required to achieve the desired clinical outcome [42, 44, 106].

Atrophic Scars

Atrophic scarring can be a result of surgery, trauma, and such common conditions as acne vulgaris and varicella (Fig 5). Many different procedures, alone and in combination, have been employed to correct these dermal depressions, which are disfiguring and may even be exacerbated by makeup due to its enhancement of textural variation.

Dermabrasion, a manual technique for removing the epidermis and a portion of the dermis that utilizes an abrasive wheel driven by a high-speed rotary engine, has long been considered the definitive treatment for atrophic and pitted scars secondary to acne [104]. The physiological basis of healing after dermabrasion rests on the capacity of the skin to regenerate its epidermal cover by epithelialization through skin appendages, primarily the pilosebaceous units. Reepithelialization takes 7 to 10 days and erythema may last for an additional 2 to 12 weeks. There is evidence that improvement in the clinical appearance of abraded skin correlates with histological evidence of new collagen formation in the dermis [107, 108]. The wider and more shallow the pits, the better the cosmetic results obtained with dermabrasion [109]. For correction of icepick or other well-demarcated scars, the results obtained with dermabrasion are enhanced when used in combination with punch excision and primary closure and/or punch grafting. During the excision or grafting, icepick scars are isolated and removed either by primary closure or replacement with a postauricular graft. The scars are then dermabraded 4 to 8 weeks later [110, 111]. Dermabrasion has also been performed in conjunction with chemical peeling for enhanced clinical results. The technique is highly operator dependent and is limited by various factors including poor visualization during surgery due to bleeding and the potential for transmission of infectious particles. Complications of dermabrasion include permanent hypopigmentation with a noticeable line of demarcation between treated and untreated skin, transient hyperpigmentation, infection, and milia formation [112].

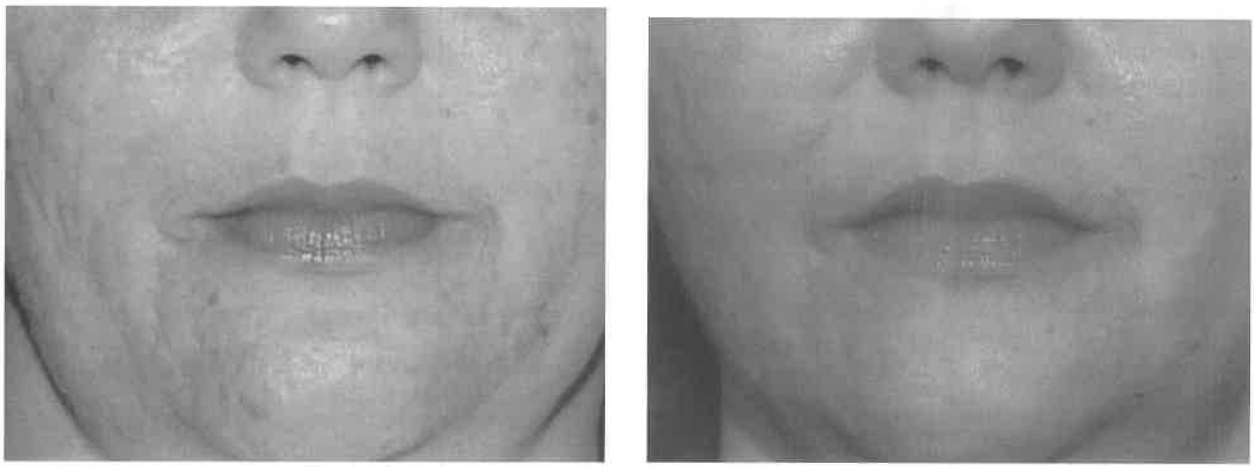
In addition to excision [109] or punch grafting [113, 114], other surgical procedures have been implemented in the correction of atrophic acne scarring. Subcision is a method of cutting under a depressed scar or contour using a tribeveled hypodermic needle, which is inserted under the skin through a needle puncture. Once beneath the defect, the surgeon attempts to raise its base manually to the level of the surrounding skin surface. The effectiveness of this technique, which may have to be repeated several times for each scar, is thought to be related to both surgical release of the fibrous strands anchoring the scar

and spontaneous fibroplasia induced by injury [115].

Tissue augmentation for depressed scars has been performed with a variety of filling materials including collagen [116–118], silicone [119], fat [120], fibrin [121, 122], and Fibrel [123]. Silicone, while proving successful in the recontouring of soft-tissue defects, produced an unacceptably large percentage of complications. Bovine collagen injection provides a relatively risk-free correction of dermal defects following adequate skin-testing procedures; however, treatment must be repeated at frequent intervals. Currently, investigators are studying various methods of harvesting and cultivating autologous collagen to avoid allergic reactions to the injected material [124]. In addition, this autologous material should remain in place for an extended duration because it is not as readily targeted by enzymes or antibodies. Fibrotic or icepick scars are not amenable to treatment with filler substances. Pinski and Roenigk [120] reported their results following autologous fat transplantation in 43 patients followed over 3 to 48 months. Cosmetic defects treated included linear morphea, expression lines, acne scars, discoid lupus erythematosus scars, and posttraumatic scars. The authors noted that the nature of the cosmetic defect was the most important factor in determining graft longevity. The greatest amount of fat resorption was encountered in treating fibrotic acne scars. Only approximately 30% of injected fat was present following 12 months. The authors proposed that the impaired vascularity of these lesions contributed to the decreased viability of the fat grafts, and postulated that the fibrosis process and not true fat cell survival was responsible for the contour improvement seen after fat transplantation. Complications included temporary swelling and minor bruising at the recipient site, and minor tenderness at the donor site [120]. There has also been a report of unilateral blindness following transplantation of autologous fat to the glabella [125].

The recent development of high-energy, pulsed, or scanned CO_2 lasers utilizing high peak powers and short pulse durations diminishes thermal conduction to normal skin structures by limiting the pulse duration to a period of time shorter than the thermal relaxation time of water-containing tissue [126–128]. The advantage of the newest, high-energy pulsed or scanned CO_2 lasers in comparison with more conventional forms of treatment lies in their ability to vaporize precisely predictable and reproducible amounts of tissue with each progressive laser pass. In a histological study comparing depth of ablation of laser resurfacing, dermabrasion, and chemical peels, Fitzpatrick and colleagues [129] demonstrated that dermal vaporization plus necrosis depth secondary to CO_2 laser resurfacing was directly proportional to pulse energy as well as the number of laser passes. Therefore, with the use of the high-energy, pulsed CO_2 laser the operator is able to remove as little or as much tissue as desired depending on the clinical situation, a distinct advantage over other resurfacing techniques [129]. Similar to dermabrasion, the mechanism of CO_2 laser resurfacing involves the regeneration of epidermis and dermis from residual appendageal structures as well as collagen remodeling, which may continue for at least 1 year following treatment. Treatment with the CO_2 laser also exerts a thermal effect on collagen that results in collagen shrinkage and may be responsible for clinical improvement following even a relatively superficial ablation [130]. Lastly, an increase in myofibroblasts within laser-induced wounds has been discovered that may provide a contracted scaffold for subsequent collagen organization [131].

Garrett and associates [132] were among the first to report cosmetically acceptable results in the treatment of acne scarring with the CO_2 laser utilizing the continuous and superpulsed modes. The computer assisted scanner that was available at that time, however, produced a depression in its footprint [132]. Later, in a report of 13 patients with skin types III and IV who underwent CO_2 laser resurfacing for acne scars, 10 patients were treated with the UltraPulse laser and 3 were treated with the Sharplan Silktouch flashscanner [133]. The authors treated the "shoulders" of scars first with one to four laser passes, followed by one laser pass to the whole cosmetic unit or vice versa. A 25% average improvement following one laser treatment was reported, with saucer-shaped scars responding better than icepick scars. These authors postulated that deeper scars would possibly show greater response to punch



A B

Fig 6. (A, B) Atrophic acne scars (A) before and (B) 6 months after high-energy, pulsed CO_2 laser resurfacing treatment.

excision or punch grafting prior to laser resurfacing. Apfelberg [134] reached similar conclusions after treating 13 patients with mild and severe acne scarring with the UltraPulse CO_2 laser over a 24-month period [134]. All patients were treated with three to five laser passes using energies of 300 to 500 mJ. He concluded that laser resurfacing of severe atrophic acne scars achieves only moderate results, while laser treatment of mild acne can provide excellent results.

In another study that included 50 patients with skin phototypes I through V and moderate to severe atrophic facial acne scars treated with a high-energy, pulsed CO_2 laser, blinded assessor ratings of clinical improvement averaged 81.4% (Fig 6). Two to five laser passes over the scarred areas were delivered using a 3-mm collimated handpiece. Skin texture analyses of the laser-irradiated scars demonstrated a return of normal skin surface markings and were comparable with those analyses obtained in normal adjacent skin. All patients were followed for 6 months with no evidence of scar recurrence or worsening [135]. On the contrary, a continued clinical improvement in atrophic scars has been observed for at least 1 year following the laser resurfacing procedure [136]. This phenomenon is probably related to ongoing collagen remodeling, which begins during the final phase of wound healing and during which the dermis responds to injury with the production of collagen and matrix proteins [137, 138]. Similar clinical results are achieved following laser resurfacing of traumatic scars.

Fortunately, side effects are uncommon following high-energy pulsed or scanned CO_2 laser surgery. Erythema, typically lasting 4 weeks to 4 months and sometimes 6 to 9 months, is expected and should not be regarded as a complication of treatment. Prolonged erythema with tissue induration and tenderness usually is indicative of early hypertrophic scarring. As has been reported with dermabrasion, the risk of scarring may be increased in patients who have been treated with oral retinoids within the preceding 2 years as well as in those patients who develop postoperative bacterial or herpetic infection [139–141]. Milia and acne may occur temporarily, especially if occlusive ointments are used postoperatively in acne-prone skin. Hyperpigmentation is not uncommon, occurring in 30% or more of patients within 4 to 6 weeks postoperatively. Although patients with olive skin tones are more likely to hyperpigment, this side effect can occur in any patient undergoing cutaneous laser resurfacing [46, 135]. Although most cases of hyperpigmentation will eventually resolve spontaneously, the fading process typically takes several months. Hypopigmentation, a common sequela of dermabrasion, has been reported infrequently as a delayed complication of laser resurfacing. It is usually not seen until several months following the laser procedure and seems to occur more

commonly in areas treated with a greater number of laser passes. In addition, areas predisposed to hypopigmentation include the oral commissures and areas of skin that have been previously treated by other modalities including dermabrasion and phenol peels. Hypopigmentation that has been commonly associated with dermabrasion may be attributed to deeper follicular melanocytic injury than what routinely occurs during laser resurfacing alone [133]. While a series of superficial chemical peels may improve the overall appearance of the skin surrounding these areas of hypopigmentation, the pigment loss appears to be permanent.

Laser resurfacing represents a major advance in the treatment armamentarium for the improvement of atrophic facial scarring. The technique is of tremendous importance to patients who suffer from the sequelae of some earlier inflammatory condition or physical trauma. While continuous-wave CO_2 lasers have been utilized for tissue vaporization for many years, their use for cutaneous resurfacing was limited by heat conduction to surrounding tissues with resultant scarring. With the advent of high-energy pulsed and scanned CO_2 laser technology, precisely controlled, layer-by-layer tissue vaporization may be achieved with minimal thermal damage to adjacent normal skin when the correct laser parameters and techniques are employed. This advance in laser technology has simplified performance of cutaneous resurfacing while minimizing adverse sequelae to the patient.

Summary

Scars are notoriously difficult to treat. Multiple treatments have been advocated in the past with varying degrees of success. Hypertrophic scars and keloids have been shown to respond to pressure therapy, intralesional steroids, systemic chemotherapy, radiation, topical silicone, and laser treatment. Simple vaporization or mechanical destruction of these proliferative scars often leads to recurrence or scar worsening.

Atrophic scars, on the other hand, respond favorably to controlled vaporization or mechanical procedures including high-energy CO_2 laser irradiation, dermabrasion, and chemical peel. More predictable and controlled depths of dermal destruction can be achieved by proper use of the latest available lasers.

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