Acne Scarring: Status Report on Treatment and Management

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Scars are an unfortunate and undesirable sequelae of acne vulgaris. As acne vulgaris is a very common disorder encountered in clinical practice, the long-lasting physical, social, and psychological effects of both the disease itself, and subsequent acne scarring when present, warrants early and aggressive treatment to mitigate the underlying inflammatory process. Contributing factors leading to acne scarring include delay in the treatment of and inadequate control of acne lesions. The type of inflammatory response and potentially genetic factors also play a role in the development of acne scars. This article reviews the pathophysiology of inflammation and the classification of acne scarring. With the advent of subtyping scars, appropriate and effective treatment protocols can be developed.

Scarring is a common sequelae of acne vulgaris, and can cause considerable frustration, emotional distress, and physical disfigurement to patients. For the clinican, treatment of acne scarring is a formidable challenge. Once scars are formed, a physical approach, such as surgical intervention, chemical peels, dermabrasion, or laser resurfacing are required to lessen the appearance of scars. Even with the best of efforts, there is no guarantee that scars will disappear, and many surgical procedures carry their own risk for scarring. In most cases, scarring appears to develop subsequent to resolution of inflammatory acne lesions; however, such lesions may be either subtle or with intense visible inflammation. *Propionibacterium acnes*, a human skin commensal bacterium, contributes to the initiation or progression of inflammation in acne vulgaris; however, other pathophysiologic mechanisms may be operative. The pathogenicity of *P acnes* stems from its ability to produce lipases and enzymes that contribute to the upregulation of proinflammatory mediators and also through stimulation of innate immune response through interaction with toll-like receptor-2. It has been suggested that an early nonspecific inflammation response is less likely to produce scarring than a response associated with a directed and delayed inflammatory cascade.[1]

Approximately 30% of patients with acne have been reported to develop acne scars.[2] Therefore, prevention, through compliant use of an effective acne treatment regimen, is the optimal method to avoid further scarring. Treatment of acne scars must be individually customized for each patient depending on the type of scar, the desired outcome, and the patient's financial situation.

Acne Scarring and Quality of Life Implications

Although the psychosocial effects of acne scarring are difficult to quantify overall, patients are capable of expressing how acne scars affect their lives. Acne scarring has been shown to exhibit a profound negative impact on the quality of life of some patients and does warrant attention by clinicians.[3] Koo[3] discusses the psychosocial effects of acne which can also be applied to acne scarring. Acne and acne scarring may lead to emotional debilitation; embarrassment; poor self-esteem; social isolation; preoccupation; low confidence; altered social interactions; anger; unemployment; exacerbation of psychiatric disease; anxiety; depression; and decreased academic performance.[3] In one study, 42% of patients stated that the impact of acne on their self-image was moderate to severe.[4] For affected adolescents, reports have shown that they experience more social isolation and self-consciousness than their unaffected peers and express more dissatisfaction with their facial appearance.[5] Patients with acne have reported that employment prospects are negatively affected and

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interpersonal relationships are also impacted adversely compared to those without acne.[6-8] The incidence of body dysmorphic disorder is higher in patients with acne than in the general population, with one report stating that body dysmorphic disorder affected 8.8% of 159 acne patients.[9] Many of those suffering from acne surprisingly do not seek immediate treatment which can prolong their psychological stress. Of those with acne, approximately 16% seek appropriate medical treatment; 74% wait more than one year before seeking evaluation; 12% wait 6 to 12 months; 6% wait 3 to 6 months; and only 7% waited less than 3 months to be seen professionally for treatment of their acne.[4] This can be attributed to many factors, including financial limitations, physician access, and patient delay, among others.

Special Considerations in Planning Treatment for Acne Scarring

There are many considerations that the clinician must be aware of before starting a treatment plan for acne scars. It is important to classify the patient's Fitzpatrick skin type before starting therapy. Fitzpatrick skin types I to II, which are lighter, typically exhibit the best response to resurfacing techniques. Fitzpatrick skin types III to IV are more likely to become transiently hyperpigmented approximately 4 to 8 weeks after resurfacing procedures, such as by laser, dermabrasion, or chemical peeling, and may exhibit hypopigmentation 12 to 18 months after resurfacing procedures.[10] Patients should also be asked about previous isotretinoin therapy. It has been suggested that patients be at least 6 to 12 months beyond isotretinoin therapy prior to acne scar treatments.[10] Isotretinoin therapy can delay reepithelization and may be associated with the development of hypertrophic scarring, although data supporting this suggested association are limited.[10] Delayed healing and an increase in the risk for infection can occur in patients with underlying bleeding disorders or immunosuppression, as well as in those who have received prior radiation therapy to the scarred area. Patients with a history of oral mucosal herpes simplex infection are best treated with prophylactic antiviral therapy prior to treatment for facial acne scarring, especially those undergoing resurfacing procedures. It is also important to discuss with patients up front that treatments for acne scarring, including surgery (ie, excision, subcision), laser resurfacing, chemical peels, and dermabrasion, are associated with potential complications, including risks for scarring and pigmentary changes that can not be predicted. Many treatments for acne scarring, such as resurfacing, excision, and subcision, have been reported to exacerbate acne and even stimulate the production of nodulocystic lesions.[11] Before performing a procedure to treat acne scarring, it is recommended that the acne be quiescent for at least 6 to 12 months.[11] In addition, it is important to obtain a personal and family history of true keloid formation as certain individuals are genetically predisposed to hypertrophic or keloidal scarring. A personal history of positivity for HLA-B14; HLA-BW16; HLA-BW35; and HLA-BW21 has been associated with scarring propensity.[12]

Pathophysiology of Inflammation

Although it has been assumed that acne scarring occurs subsequent to visible resolution of deep inflammatory acne lesions, scarring may result at sites previously affected by superficial inflammatory acne lesions, even when visible inflammation is minimal. In some cases, postinflammatory erythema, which is commonly seen in fair-skinned individuals and may take months to fade after resolution of palpable inflammatory acne lesions, is often confused with acne scars by patients (Figure 1). The presence of scarring at these sites is variable and is best evaluated after the erythema fades. In addition, certain clinical subtypes of acne, such as acne fulminans and acne conglobata, have a propensity to scar after lesions heal.

In the generation of inflammatory lesions, proliferation of *P acnes* in the affected pilosebaceous units is believed to be critical, and is instrumental in the production of the inflammatory stage of acne and may play a role in increasing the risk for scarring.[13] Inflammation in acne lesions leads to the thinning of the follicular wall, and once this wall is breached, there is extravasation of follicular contents that are foreign to the dermis. Although the inflammatory process of acne is initiated prior to follicular wall rupture, with loss of follicular wall integrity there is an amplification of the intensity of perifollicular and follicular inflammation. The role of *P acnes* is also

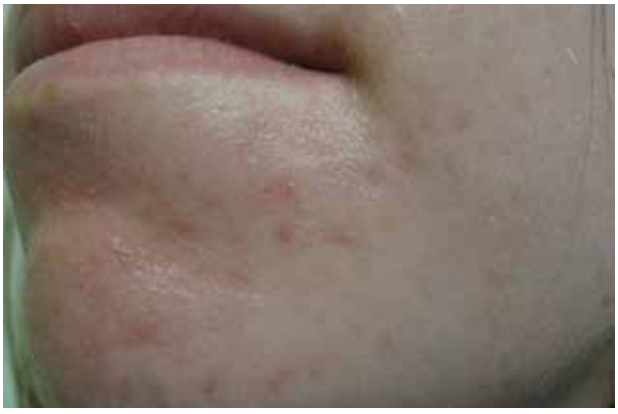

Figure 1. Patient with postinflammatory erythema that is often confused with acne scarring.

believed to intensify after dermal exposure with activation of both classic and alternative complement pathways.[14] If a host response results in incomplete containment of the perifollicular inflammatory process, follicular rupture and spillage progresses further, potentially leading to formation of multichanneled fistulous tracts.[14] The end result after inflammation dissipates are clinically apparent, grouped, open comedones, ice-pick scars, or both.[15]

Scars owe their appearance to the extent and the depth of inflammation. If inflammation extends markedly into the dermis, matrix degradation is significant, with a greater potential for subsequent dermal scarring. Damage to collagen and other dermal matrix components secondary to inflammation of acne leads to fibrosis and permanent changes in skin texture. Over the next several months, the wound undergoes remodeling with deposition of new matrix and collagen synthesis. In contrast, damage limited to the epidermis or papillary dermis will usually heal without scar formation.[4] Epidermal damage results in more transient erythema or pigmentary changes, without development of scars. Ultimately, the amount, type, and depth of scarring are dependent on the location, nature, and intensity of the response to inflammation of the individual host.

Pathophysiology of Acne Scarring

Acne scars can be broadly categorized into 2 main groups; scars characterized by tissue loss (atrophic) and scars characterized by tissue excess (hypertrophic or keloidal). Atrophic acne scars, which are secondary to destruction and dissolution of supporting dermal tissues, are more common than hypertrophic acne scars.[10] Although the majority of acne scars are atrophic, there is a propensity for some individuals to develop hypertrophic and keloidal scars. Melanocytes have been suggested to play a role in scar formation, with darker-skinned individuals having a greater propensity to form scars and keloids, and with the absence of ability to develop keloids observed in patients with oculocutaneous albinism. Mast cells are noted to be numerous in hypertrophic scars and keloids and also play a role in excessive deposition of collagen and upregulation of collagen synthesis. Transforming growth factor β (TGF-β) has emerged as a likely culprit for inducing scar and keloid formation, and TGF-β1 and TGF-β2 are highly expressed in keloid-derived fibroblasts as compared with normal control fibroblasts.[16] The injection of TGF-β1 into athymic mice has been shown to lead to the formation of keloid-like nodules.[17] It is not entirely clear how these pathophysiologic mechanisms correlate with acne scarring.

According to an in vivo study, the transcription factors nuclear factor-κB (NF-κB) and activator protein-1 (AP-1) are activated in acne lesions, leading to the elevation of target gene products, inflammatory cytokines, and matrix-degrading metalloproteinase (MMP) enzymes.[18] MMPs are zinc-dependent enzymes that are involved in many inflammatory diseases, wound healing, and wound remodeling. These resultant gene products are molecular mediators of inflammation and collagen degradation in acne lesions in vivo.[18] An important transcription factor involved in inflammation, AP-1 is also activated in severe acne lesions.[18] A consequence of AP-1 activation is enhanced transcription of AP-1–regulated genes, which increase production of several MMPs, such as MMP-1 (collagenase 1 or interstitial collagenase); MMP-8 (collagenase 2 or neutrophil collagenase); MMP-9 (92-κDa gelatinase of collagenase 4); and MMP-13 (collagenase 3).[19] MMP-1 is critical in the degradation of mature collagen and initiation of site-specific cleavage within the triple-helical domain of type I and other fibrillar collagens.[19] MMP-8 and MMP-13 are also collagenases that may degrade collagen. In inflammatory acne lesions, MMP-1, MMP-3, and MMP-9 are elevated as compared with uninvolved facial controls.[18] MMP-1 (interstitial collagenase), MMP-8 (neutrophil collagenase), and MMP-13 (collagenase-3), can degrade native fibrillar type I and type III collagen.[18,19] MMP-8 (neutrophil collagenase) is highly active against type I collagen and is produced by polymorphonuclear neutrophils (PMNs); it is also stored within the cell.[18,19] A consequence of PMN infiltration into tissue is delivery of MMP-8 to the site where it is secreted, which can contribute to dermal matrix degradation. The degradation of dermal supporting tissue is followed by synthesis and repair of new collagen and dermal matrix, which may sometimes be random and imperfect.[18] If this cycle of upregulation of MMP and procollagen synthesis is sustained over time, acne scarring may become clinically noticeable.[18] On the other hand, the organization and composition of the extracellular matrix in the wound-healing process could leave clinically undetectable defects; therefore, no scar would be seen.[18] The ability to target matrix remodeling and decrease the inflammatory cascade has been a major goal of current acne therapies and is implicated in future treatments directed against development of acne scars.

Topical and Injectable Treatments for Acne Scars

Topical treatments or injectables that have been suggested for prevention or treatment of scarring include vitamins A, E, C; zinc; colchicines; corticosteroids; hyaluronidase; cyclosporine; honey; onion extract; 5-fluorouracil; bleomycin; retinoids; verapamil; pepsin; hydrochloric

acid; and formalin.[20-22] However, data supporting most of these approaches specifically for acne scarring are limited. Vitamin E is a major lipophilic antioxidant in plasma, membranes, and tissues, and has been used for its anti-inflammatory effects. Vitamin C is also known to have anti-inflammatory activity. Topical vitamin C has been shown to enhance collagen production in human skin and has also been reported to stimulate collagen synthesis and stabilize procollagen mRNA. In addition, increased levels of tissue inhibitor of MMP-1 have been observed, suggesting that topical vitamin C may mitigate collagen breakdown, whereas mRNA levels of elastin, fibrillin, and tissue inhibitor of MMP-2 remain unchanged. MMPs, whose role in modulating the dermal matrix is previously discussed, are zinc-dependent proteases that are involved in the formation of the extracellular matrix. Zinc is an element that is required in wound healing, and has been shown to reduce the cellular and genetic damage caused by oxidative stress and enhance resistance to skin fibroblasts. Topical retinoids have been used to improve the appearance of keloids, hypertrophic scars, and superficial scars.[20,21] The benefits are attributed to an increase in elasticity and dermal collagen deposition with proper structural alignment.[21] Intralesional corticosteroid injection can be used for hypertophic scars and keloids.[22] Corticosteroids exhibit multiple immunomodulatory and anti-inflammatory properties that reduce the expression of cytokines, cellular adhesion molecules, and other enzymes related to the inflammatory cascade.[22] Intralesional triamcinolone injections can help to decrease the production of collagen, decrease inflammation, and stimulate collagen resorption.[22]

Classification System of Acne Scars

There are 3 basic types of atrophic scars that have been described by Jacob et al.[23] Each category may require different or multiple therapeutic modalities.[23,24] Types of atrophic acne scars include ice-pick scars, rolling scars, and boxcar scars. Ice-pick scars are narrow (<2 mm), v-shaped, deep, sharply marginated epithelial tracts that extend vertically to the deep dermis or subcutaneous tissue. The depth reaches below conventional skin resurfacing options.[24] Rolling scars occur from dermal tethering, with abnormal fibrous anchoring of the dermis to the subcutis leading to superficial shadowing. Rolling scars are usually wider than 4 to 5 mm and although they are shallow, the subdermal tether precludes treatment from the surface above. Figure 2 shows both ice-pick and rolling acne scars on a 19-year-old female patient. Boxcar scars have a flat, u-shaped base with sharply demarcated vertical edges, similar to varicella scars. Broader than ice-pick scars, they are round, polygonal, or linear at the skin's surface. They can be shallow (0.1–0.5 mm) or deep (>0.5 mm). Shallow boxcar scars are within the dermal reach of skin resurfacing treatments, but deeper boxcar scars are resistant to improvement in the absence of full-thickness treatment of the scar.[25]

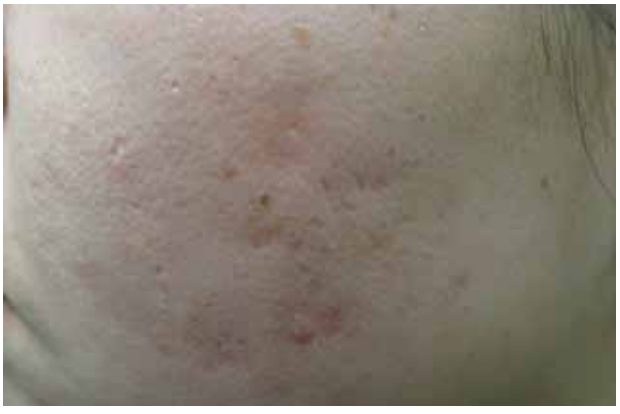

Figure 2. A 19-year-old female patient with ice-pick scars and rolling scars resulting from acne.

Hypertrophic acne scars result from excess proliferation of fibrous tissue, and may be hypertrophic or keloidal in nature.[23,24] Hypertropic acne scars remain reasonably within the confines of the preexisting acne lesion. Keloidal acne scars extend significantly beyond the original site of the preexisting acne lesion. Figure 3 shows both hypertrophic and keloidal acne scarring on the chest of a 20-year-old male.

Surgical Management of Acne Scars

Surgical management is the best route for ice-pick, rolling, and boxcar scars. Ice-pick scars can be treated by punch excision, punch grafting, or both. Rolling scars can be treated with subcision, radiofrequency ablation, nonablative laser resurfacing, appropriate dermal filler substances, and dermal grafting. Boxcar scars can be treated with ablative laser resurfacing, dermabrasion, excision, punch elevation, punch grafting, and chemical peels. Punch techniques are used for scars with very atrophic bases or sharply punched out ice-pick scars. The defect is then allowed to heal by second intent, or closed with sutures. The surgical choice for rolling or depressed scars (not for ice-pick or atrophic scars) is subcision. A tri-bevel needle is probed under the lesion through the needle puncture site so it is not a true incision. This movement releases papillary skin from the binding connections of the deeper tissue. This creates controlled trauma that leads to wound healing and associated additional connective tissue formation in the treated location.

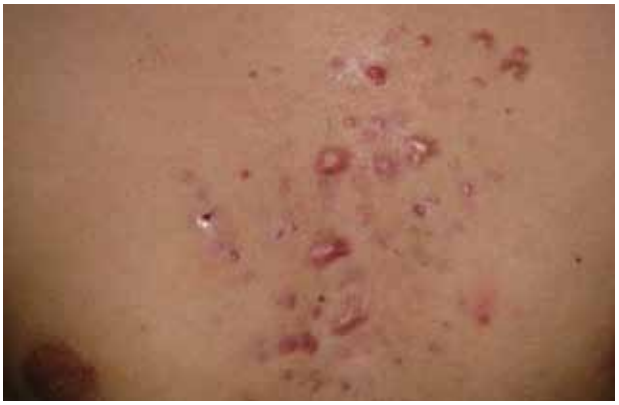

Figure 3. A 20-year-old male with hypertrophic and keloidal acne scarring on the chest.

Laser Resurfacing for Acne Scars

Lasers for skin resurfacing were initially described in 1989. Today, when appropriately applied, they are highly effective in treating atrophic acne scars.[23] Both ablative and nonablative lasers are used for treatment of acne scarring. Ablative lasers include CO_2, erbium:YAG, and Fraxel lasers. These lasers emit high-energy pulses of light to remove thin layers of skin, with little thermal damage to the adjacent tissue. Ablative lasers produce epidermal ablation, thermal contraction of the dermis, upregulate type I collagen fibers, and promote dermal remodeling.[10] Distensible, undulated acne scars respond better to ablative effects of the CO_2 laser because the more extensive thermal injury produces greater collagen shrinkage and skin tightening.[10]

Conclusion

Early and effective treatment of acne is the best route to prevent scarring and to minimize the social, physical, and psychological effects of acne. Acne scarring significantly impacts the lives of many patients in adverse ways and should be addressed by clinicians early in the course of acne management. Acne is capable of producing psychological problems and physical scarring, both of which correlate with the duration of the disease, suggesting the importance of early intervention. The importance of strict adherence to the medical regimen should be addressed with the patient up front. After acne is quiescent, the approach must be tailored to the patient's desired outcome, skin type, genetic propensity to scar, and the subtypes of scars that are present. Additionally, patients must know that improvement in scarring will not be 100%, and that multiple treatments may be needed to ultimately achieve a reasonable overall result. In conclusion, acne scarring is a complex problem that may require a combination of several procedures, requiring close alliance with the patient during this often long and frustrating journey.

References

1. Holland DB, Jeremy AH, Roberts SG, et al. Inflammation in acne scarring: a comparison of the responses in lesions from patients prone and not prone to scar. *Br J Dermatol*. 2004;150:72-81.
2. Cunliffe WJ. The sebaceous gland and acne—40 years on. *Dermatology*. 1998;196:9-15.
3. Koo J. The psychosocial impact of acne: patients' perceptions. *J Am Acad Dermatol*. 1995;32:S26-S30.
4. Tan JK, Vasey K, Fung KY. Beliefs and perceptions of patients with acne. *J Am Acad Dermatol*. 2001;44:439-445.
5. Schachter RJ, Pantel ES, Glassman GM, et al. Acne vulgaris and psychologic impact on high school students. *N Y State J Med*. 1971;71:2886-2890.
6. Cunliffe WJ. Acne and unemployment. *Br J Dermatol*. 1986;115:386.
7. Layton AM. Acne scarring: reviewing the need for early treatment of acne. *J Dermatol Treat*. 2000;11:3-6.
8. Jowett S, Ryan T. Skin disease and handicap: an analysis of the impact of skin conditions. *Soc Sci Med*. 1985;20:425-429.
9. Uzun O, Başoğlu C, Akar A, et al. Body dysmorphic disorder in patients with acne. *Compr Psychiatry*. 2003;44:415-419.
10. Frith M, Harmon CB. Acne scarring: current treatment options. *Dermatol Nurs*. 2006;18:139-142.
11. Alam M, Dover JS. Treatment of acne scarring. *Skin Therapy Lett*. 2006;11:7-9.
12. Oluwasanmi JO, Otusanya MO. Human leucocyte antigens (HLA) and keloids. *W Afr J Med*. 1983;2:127-130.
13. Goodman G. Acne and acne scarring—the case for active and early intervention. *Australian Fam Physician*. 2006;35:503-504.
14. Webster GF, Leyden JJ, Nilsson UR. Complement activation in acne vulgaris: consumption of complement by comedones. *Infect Immun*. 1979;26:183-186.
15. Strauss JS. Sebaceous glands. In: Fitzpatrick TB, Eisen AZ, Wolff K, et al, eds. *Dermatology in General Medicine*. 4th ed. New York, NY: McGraw-Hill; 1993:709-726.
16. Smith P, Mosiello G, Deluca L, et al. TGF-beta2 activates proliferative scar fibroblasts. *J Surg Res*. 1999;82:319-323.
17. Campaner AB, Ferreira LM, Gragnani A, et al. Upregulation of TGF-beta1 expression may be necessary but is not sufficient for excessive scarring. *J Invest Dermatol*. 2006;126:1168-1176.
18. Kang S, Cho S, Chung JH, et al. Inflammation and extracellular matrix degradation mediated by activated transcription factors nuclear factor-kappaB and activator protein-1 in inflammatory acne lesions in vivo. *Am J Pathol*. 2005;166:1691-1699.
19. Birkedal-Hansen H, Moore WG, Bodden MK, et al. Matrix metalloproteinases: a review. *Crit Rev Oral Biol Med*. 1993;4:197-250.
20. Orringer JS, Kang S, Johnson TM, et al. Tretinoin treatment before carbon-dioxide laser resurfacing: a clinical and biochemical analysis. *J Am Acad Dermatol*. 2004;51:940-946.
21. Berardesca E, Gabba P, Farinelli N, et al. In vivo tretinoin-induced changes in skin mechanical properties. *Br J Dermatol*. 1990;122:525-529.
22. Jalali M, Bayat A. Current use of steroids in management of abnormal raised skin scars. *Surgeon*. 2007;5:175-180.
23. Jacob CI, Dover JS, Kaminer MS. Acne scarring: a classification system and review of treatment options. *J Am Acad Dermatol*. 2001;45:109-117.
24. Jemec GB, Jemec B. Acne: treatment of scars. *Clin Dermatol*. 2004;22:434-438.
25. Bayat A, McGrouther DA, Ferguson MW. Skin scarring. *BMJ*. 2003;326:88-92.