
Hypertrophic Scars

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For decades, hypertrophic scarring, contraction, and pigment abnormalities have altered the future for children and adults after thermal injury. The hard, raised, red and itchy scars; shrunken wounds; and hyper- and hypo-pigmented scars are devastating to physical and psychosocial outcomes. The specific causes remain essentially unknown and, at present, prevention and treatment are symptomatic and marginal at best.

BACKGROUND

Hypertrophic scarring is the major significant negative outcome after survival from of a thermal injury. Hypertrophic scars are hard, raised, red, itchy, tender, and contracted.^{1,2} These scars are ugly, disfiguring, and uncomfortable and may diminish, but never totally go away.

Hypertrophic scarring after deep partial-thickness wounds is common. We have reviewed the English literature on the prevalence of hypertrophic scarring³ and found that children, young adults, and people with darker, more pigmented skin are particularly vulnerable and, in this subpopulation, the prevalence is up to 75%.⁴⁻⁶

Hypertrophic scarring is devastating and can result in disfigurement and scarring that affects quality of life which, in turn, can lead to lowered self esteem, social isolation, prejudicial societal reactions, and job discrimination.⁷⁻¹² Scarring also has profound rehabilitation consequences, including loss of function,

impairment, disability, and difficulties pursuing recreational and vocational pursuits.^{10,13,14}

Essentially the same can be said about wound contraction and hyper- and hypopigmentation after thermal injury. They are significant negative outcomes, common and devastating.^{15,16}

WHAT IS NOT KNOWN

Problems With the Current State of Clinical Science

The current understanding of postburn scarring is deficient in many aspects. There are no useful, objective definitions that consistently distinguish between atrophic, wide, normotrophic and hypertrophic scars and keloids.¹⁷ This means that, in research studies, scars are grouped on a clinical basis, which undoubtedly varies from provider to provider. The result is confusing results and incomplete answers.

We have neither a standardized method to measure the severity of hypertrophic scar nor an objective reproducible method to measure the response to treatment. Several methods have been suggested, including clinical observation, Vancouver Burn Scar Scale, scar volume, photography, vascularity, pliability, and ultrasound thickness.¹⁸⁻²⁵ None of these methods cover the entire problem, and none has been accepted as the standard.

Our knowledge of incidence and socioeconomic impact of hypertrophic scar is minimal. We do not know the answers to the following questions^{3-6,26}:

- What is the frequency after thermal injury?
- How great is the socioeconomic impact?
- Who is more likely to develop hypertrophic scars given similar severity of initial injury?
- How does age, sex, and race/origin affect the development of hypertrophic scar?
- What is the psychological impact to the surviving burn patient?

We are unable to determine which scars will become hypertrophic.²⁷ Our understanding of the pathophysiology of hypertrophic scarring is limited, both locally and systemic. Hundreds of studies of human hypertro-

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phic scars have been performed during the past decades, but the pathophysiology of hypertrophic scarring is still only partially understood.^{28–37}

- What is the role of burn depth in the development of hypertrophic scarring?
- How does the treatment affect the development of hypertrophic scar?
- How does the timing of wound closure affect the subsequent development of hypertrophic scarring?

There is essentially no known completely effective method of prevention and/or treatment of hypertrophic scarring. Pressure garments, silicone sheeting, steroid injections, and various other treatments have been tried but none prevent and/or solves the problem.^{33,38–43} This leaves reconstructive plastic surgery as the sole option, which usually is performed months after the appearance of hypertrophic scars exposing the patient to a long period of discomfort and misery and imposing upon the patient and society the resultant financial and social burden. The same general statements can be made regarding contraction and pigment alterations.

Problems With the Current State of Laboratory Science

Our current understanding of the cause of hypertrophic scarring is very incomplete. For example, although the abnormalities in ultrastructure and cellular and extracellular matrix in hypertrophic scar are partially understood, the factors that drive the development of these lesions remain elusive. One reason that the etiology of human hypertrophic scar is unknown is the absence of a useful animal model.^{36,44–47} Despite numerous attempts by multiple investigators, mice, rats, rabbits, dogs, and cats have all failed to produce scars analogous to human hypertrophic scars. Repetitive literature searches have yielded few references to animal models of hypertrophic scar. Morris⁴⁵ reported a scar model in the rabbit ear. We found only a limited number of studies from other investigators utilizing this model to study scar³⁹ and it is a small, full-thickness wound, which is quite different from the large, partial-thickness burn wounds in which the deep dermis remains that leads to the development of hypertrophic scar. Human hypertrophic scar tissue has also been implanted into athymic rats and mice.^{46,48–54} These models have been used in two studies by other groups^{55,56} but seem very dissimilar to the clinical situation and the tissue implanted is established scar so any early changes are missed. Aksoy et al³⁶ described a hypertrophic scar model in the albino, male guinea pig after excision of the panniculus carnosus and development

of flaps, application of thermal injury, and treatment with coal tar. We could find no further use of this model. The Duroc/Yorkshire animal model of fibroproliferative scarring has received some recent attention as has burn wounds in the Large White pig.^{37,57–71}

Without a representative animal model of human hypertrophic scar, scar tissue for study is usually obtained from humans undergoing scar revision that is done many months after the scar first developed. Time is an important variable in wound repair,³⁴ and it is known that gene expression may be early and transient during wound repair.⁷² This early expression, which likely determines the pathology of hypertrophic scar weeks and months later, may be missed by our current strategies that include biopsies of established hypertrophic scar. Earlier investigation of the developing scar is likely to be essential to understanding the fibrotic process.

A second reason for our lack of knowledge regarding hypertrophic scar may be that scars of varying ages often are aggregated into a few large categories, for example, less than 12 months, 12 to 24 months, and greater than 24 months. As mentioned previously, time is an important variable in wound repair and collapsing the time axis into large calendar blocks may hide the biologic events.

A third reason for our lack of understanding of the etiology of hypertrophic scarring is that, in the past, most human hypertrophic scar tissue for study has been minced and homogenized. This action destroys skin anatomy and homogenizes all cell populations. This seems inappropriate because signaling in the epidermis may be differentially regulated compared with the deep dermis. Mesenchymal–epithelial cell interactions and potential signaling cues that may regulate scarring may be masked. Laser microdissection is now possible and can be used to study different anatomic portions of scar such as the deep residual uninjured dermis and the more superficial scar mass. It also can be used to separate the collagen mass from the skin appendages, cone structures and other intrinsic structures of the skin.^{57,58,73}

CONCLUSION: PROPOSED RESEARCH PRIORITIES

We propose five priorities (Table 1) to move our understanding of hypertrophic scarring, contraction, and pigment alteration after thermal injury forward.

Priority 1: Early and Serial Biopsies

Typically studies are performed with samples obtained during scar revision, which means they are ob-

Table 1. Priorities for research on scars

- Study of early and serial scar biopsies
- Study of microdissected scar samples that separate and differentiate hypodermis, dermis, superficial scar and epidermis
- Studies of wounds that healed spontaneously
- Definition of atrophic, wide, normotrophic and hypertrophic scars
- Studies on the incidence and socioeconomic impact of scar

tained months/years after the process began. We need samples of normal skin and shallow and deep wounds obtained in the first days and weeks after injury. Ideally, these should be in the same individual to reduce the variability in wound healing that exists between individuals. Therefore we need a standardized animal model of this process and patient and human subjects permission to biopsy burn wounds early and serially after injury.

Priority 2: Microdissected Samples

Studies usually are done with homogenized samples. This means that any hypodermis and dermis are ground up with the scar and any differences are lost. Future studies need to separate and differentiate between residual hypodermis and dermis and the superficial scar mass and the new epidermis. Laser microdissection may permit this procedure.

Priority 3: Studies of Wounds That Healed Spontaneously

Hypertrophic scarring often follows spontaneous healing and is likely significantly altered by excision and grafting. Therefore, the studies should include wounds that were not excised and grafted and consequently some small deep partial-thickness and full-thickness wounds may need to be permitted to heal over time and not excised and grafted.

Priority 4: Definition of Atrophic, Wide, Normotrophic, and Hypertrophic Scars

At present, the definition of each of these is basically clinical. We need to characterize each of these with objective, biologic markers, which may be determined by Priorities 1–3.

Priority 5: Incidence and Socioeconomic Impact

The incidence of these problems is not known with accuracy nor is it stratified by age, sex and race/origin. As a result, we cannot estimate the socioeconomic impact. We need this data to obtain funding for the study of these problems.

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