Advances in Ophthalmology and Optometry 1 (2016) 165–179

ADVANCES IN OPHTHALMOLOGY AND OPTOMETRY

Scar Modulation

Kian Eftekhari, MD[a],
Raymond S. Douglas, MD, PhD[b], Guy G. Massry, MD[c,d,*]

[a]Oculoplastic Surgery, Inc, 1002 East South Temple, Suite 308, Salt Lake City, UT 84102, USA; [b]Division of Eye Plastic, Orbital, and Facial Cosmetic Surgery, Department of Ophthalmology and Visual Sciences, Kellogg Eye Center, University of Michigan Medical School, University of Michigan, 7120 Brehm Tower, 1000 Wall Street, Ann Arbor, MI 48105, USA; [c]Division of Oculoplastic Surgery, Department of Ophthalmology, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA; [d]Beverly Hills Ophthalmic Plastic and Reconstructive Surgery, 150 North Robertson Boulevard # 314, Beverly Hills, CA 90211

Keywords

• Wound healing • Hypertrophic scar • Keloid • Scar revision • Triamcinolone • 5-Fluorouracil • Microporous annealed particle gels

Key points

- Wound healing involves diverse and overlapping phases of inflammation, followed by granulation and remodeling.
- Fetal wound healing may have implications for adult scar modulation.
- Scar revision surgery may be useful if the scar is perpendicular to relaxed skin tension lines.
- Intralesional injections of 5-fluorouracil with or without triamcinolone may improve scar appearance.
- Neurotoxins, dermal fillers, and newer therapies on the horizon may further improve scar appearance.

INTRODUCTION

The skin's response to surgical or traumatic injury leads to a cascade of events resulting in the formation of a scar. Wound healing occurs via complex mechanisms involving an initial inflammatory response, followed by deposition of collagen, and last, by tissue remodeling. The type of wound that results is

Disclosure Statement: The authors have nothing to disclose.

*Corresponding author. Beverly Hills Ophthalmic Plastic and Reconstructive Surgery, 150 North Robertson Boulevard # 314, Beverly Hills, CA 90211. *E-mail address*: gmassry@drmassry.com

2452-1760/16/$ – see front matter
http://dx.doi.org/10.1016/j.yaoo.2016.03.002

affected by many factors, including the arterial blood supply to the wound site, which may be impaired by vascular disease (diabetes, connective tissue disease) as well as other factors such as age and the presence of infection [1].

STAGES OF WOUND HEALING

Adult wound healing occurs via a series of responses to trauma that occur in stages. Initially, an acute inflammatory response occurs in which a fibrin clot is formed and neutrophils predominate. In the first 1 to 2 days after injury, inflammatory cells produce the cytokines that set up the later stages of wound healing; this is followed by macrophage migration that clears out the inflammatory debris. Macrophages also lead to the secretion of growth factors, which recruit and activate fibroblasts at the wound site. Fibroblasts mediate the formation of granulation tissue, including the formation of new blood vessels. This angiogenesis is primarily driven by vascular endothelial growth factor. Granulation tissue also is composed of glycosaminoglycans and both type I and type III collagen. In early scar formation, type III collagen predominates; in a mature scar, type I collagen predominates. The scar re-epithelializes via keratinocyte proliferation.

In the phase of fibroblast proliferation, certain fibroblasts differentiate to myofibroblasts with resultant wound contraction. This response may lead to unsightly scars, which may be modified with the use of neurotoxin. Finally, wound remodeling occurs in which matrix metalloproteinases remodel the fibrous and collagen components of the developing scar; this is characterized by a turnover of collagen in which new type I collagen is formed while older, type III collagen is degraded, which increases the tensile strength of the wound. This constant turnover of collagen in the mature scar may be a reason scar modulation is possible in a mature wound.

FETAL WOUND HEALING

One of the mysteries of wound healing is the fact that fetal wounds mature without scar formation [2]. Several theories explain this difference in fetal and adult wound maturation, including the contents of the extracellular matrix (ECM) and a lengthier presence of hyaluronic acid (HA) in the fetal wound [3]. When wound injury occurs under experimental conditions in the fetus, the skin wound heals with normal tissue architecture and skin appendages, including hair follicles and sebaceous glands, which does not occur in adult wound healing [4]. In addition to the increased presence of HA in the ECM of the fetal wound, there is less neovascularization and minimal inflammation. The mechanisms underlying scarless fetal wound healing have not been completely elucidated, but appear to be related to factors inherent to the fetal skin, as adult skin transplanted into the fetal milieu results in formation of a scar. Conversely, fetal skin transplanted into a subcutaneous location of injured skin in an adult results in scarless wound healing [4]. This effect of scarless fetal wound healing ends at around 24 weeks gestation in the human fetus, suggesting a temporary nature as the transition to an adult would-healing phenotype