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Review Article

Understanding of Scar Less Wound Healing

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Abstract

When the scalper goes on skin a wound is created that activates various systems including the endocrine system, and repairing of wound starts. During this process every event and the environment should be so precise then healing will be scar less. Wound healing is so time consuming and complex that proper and precise understanding is obscure. Many researchers have advocated on the involvement of hormones In this process, Estrogen is a steroid sex hormone and performs diverse functions in the bone, adipose tissue, skin, hair, brain, skeletal muscle and cardiovascular system and takes part in collagen synthesis; among these many are involved wound healing. It acts specifically via its own receptors in both genomic and nongenomic pathways. In this short review we have hypothesized the application of this multifunctional hormone to achieve scar less wound healing.

Keywords: In utero surgeries, Oral wounds, Skin, Keratins, Collagens, Keloids, Proteoglycans

Introduction

Wound healing is a physiological process to maintain the integrity of skin after trauma, either by accident or by procedure. Any disruption or unbalanced distribution of these processes might result in abnormal wound healing [1-3]. Lately, human fetal surgery is successfully performed, albeit, in a small number. Following surgical repair, fetal wounds heal without scarring. Cuts inside the mouth heal faster than cuts on the body; they tend to heal on their own, without stitches. Generally, oral wounds heal faster, may be due to the rich blood supply in the face and mouth help speed recovery. In the adult oral mucosa healing provides the closest example to fetal scar less healing. Injuries to the oral mucosa heal with very minimal scarring. Scar less wounds remain challenging despite the development of various therapeutic regimens owing to the complex wound healing mechanism. The therapeutic strategies that are being employed so far for wound healing based on wound types and intrinsic regenera-

tive capacity include modern hydrogels wound dressings [4] topical drug and growth factor delivery [5] hyperbaric oxygen therapy [6] auto/allograft and xenograft [7,8].

Scar formation

If the wound is not healing in a normal way, it may take the turn and follow either pathway: in one pathway it forms hypertrophic scar where the growth does not extend beyond the wound margins and there is no recurrence even after new excision. On the other hand, keloid can either develop spontaneously or may develop response to injury. The growth generally extends beyond the wound margins and recurs on excision [1].

A surgical wound is a cut or incision in the skin that is usually made by a scalpel during surgery. A surgical wound can also be the result of a drain placed during surgery. Surgical wounds vary greatly in size. They are usually closed with

sutures, but are sometimes left open to heal.

Any surgery that involves an incision will always leave a scar – the formation of scars is a normal part of the body's healing process. Scars never completely disappear, but they fade over time. Surgical wounds are made in a sterile environment where many variables can be controlled such as bacteria, size, location and the nature of the wound itself. Clean cuts can heal very well if they're washed out and treated to avoid infection. Scar tissue growth can be reduced to some extent after surgery by covering the scar and applying sunscreen if you have to go outside. Always stay hydrated and well-nourished with adequate protein and vitamins. . Avoid smoking, as nicotine restricts blood flow and slows scar healing. Manage any chronic conditions, such as diabetes, carefully. Studies have shown that silicone can help reduce scarring and is commonly used after plastic surgery [9].

Differences Between Fetal and Adult Wounds

Important differences between adult wounds have many inflammatory cells whereas fetal wounds have few or no inflammatory cells [10,11]. Hyaluronic acid, which promotes cellular movement, is present in large amounts in fetal wounds; on the contrary in adults it is found in low quantities resulting in inhibition of cellular movement [12,13]. Immature mast cells are low in numbers in fetal wounds compared to adult wounds, in adults mast cell are fully mature [14,15,], on the contrary stem cells are more in embryonic stage and less in adults [16] In both cases collagens Type III and Type I are present but in the reverse ratios [14,17] whereas keratin K8 K19 are present in fetal wounds but absent in adults [11,18]. TGF- β [16,18, 19] in fetal Low expression of TGF- β where as in adult there is a high expression of TGF- β , Way back Rinkevich et al. [20] reported a population of fibroblasts, defined by embryonic expression of the gene engrailed 1 (En1) that are responsible for the production of normal and scar collagen in the dorsal skin of adult mice.

Scar Formation

Fibroblasts, the primary mesenchymal cell type in skin dermis, play a key role in synthesizing collagens and elastic fibers within the extracellular matrix in connective tissue participate in scar formation hence play a regulatory role in the process; Scars develop in all shapes and sizes; some are large and painful, while some are barely visible.

Scar tissue is made primarily of a protein called collagen. A proteoglycan, (decorin) widely distributed in many connective tissues, may have functions in regulating collagen fibril. Studies have shown that estrogen supports collagen production by binding to receptors in the skin known as fibroblasts [21]. Fibroblasts are responsible for producing collagen the protein which gives skin its strength and flexibility and elastin-the protein which allows stretched skin to return to its original shape. proteoglycans play a significant role in wound

healing; however, scar formation Proteoglycans participate in cell-cell and cell-matrix interactions, cell proliferation, and migration, and in cytokine and growth factor signaling associated with wound healing [2,3, 21]. Specific interactions between proteoglycans (through both their glycosaminoglycan and core protein components) and macromolecules in the extracellular matrix are the key factors in the functions of proteoglycans. Exciting biological functions of proteoglycans are now gradually emerging [22].

During pregnancy cardiac output doubles, with a resulting increase in peripheral blood flow due to which wound healing may well be enhanced. Throughout pregnancy, the uterus becomes up to 500 times larger than its normal size. Once the placenta is removed, the uterine involution takes place. After childbirth, the placenta leaves behind a wound the size of a dinner plate inside the uterus. By the six-week mark, the vagina, perineum or C-section incision should be healed, and the uterus should be back to its normal size. Throughout those first weeks, mothers experience a lot of changes – from new levels of tiredness to hormone fluctuations [23].

The fetus is bathed in amniotic fluid rich in growth factors such as IGF-1 and EGF and heals skin wounds quickly with little scar tissue. Uterine wound healing process involves many cells namely, endothelial cells, neutrophils, monocytes / macrophages, lymphocytes, fibroblasts, myometrial cells as well a stem cell population found in the myometrium, myoSP (side population of myometrial cells). In contrast to adult wound healing, the early gestation fetus has the remarkable ability to heal skin wounds without scar. This observation was first reported more than three decades ago and has subsequently been confirmed in both animal models and human fetuses. The wound healing properties of adult and fetal skin tissues differ substantially. While adult cutaneous wounds heal more slowly and are accompanied by scar formation, the fetal tissue is characterized by rapid and scar less wound healing [24]. Scar less healing in the fetus is characterized by regeneration of an organized dermis with normal appendages and by a relative lack of inflammation. Surgical scars are typically raised (hypertrophic) at first but often flatten on their own within the first year such scars are known as cicatrix. While it varies from person to person, on average, surgical scars will fade from reddish (in the early stages of formation) to pink or flesh-colored in seven months. Some scars may take up to two years to become less noticeable. Keloids, a type of hypertrophic scar, can also develop during the healing process and may take up to a year to form. Unlike typical raised scars, keloids will not go away on their own [25,26]. Surgery scars are inevitable, regardless of surgeon's skill, the reason for surgery, or where the incision is located. However, there are steps during the recovery period that may help to minimize or prevent scarring.

Risk Factors for Scarring

Identified risk factors for hypertrophic scar development include age, gender, pigmentation of skin, neck or upper limb burns, multiple surgical procedures, healing greater than 3 weeks, meshed skin graft use, and burn severity [27]

Age: Aging skin becomes thinner and less elastic. That is because collagen (which makes the skin flexible) reduces with age. This change results in the fat layer under the skin. Therefore, skin does not heal as well or as quickly as we age.

Race: Some races are prone to scar. For example, people of African descent are more likely to form hypertrophic and keloid scars. In addition to the race gender also play a pivotal role in keloid formation [28]

Genetics: Genetics plays a significant role in determining an individual's predisposition to certain types of scarring. The genes responsible for collagen production, inflammatory response and tissue remodeling can influence the scar formation process.

Steroid Treatment

Most scars fade over time and never cause long-term health problems. How a scar changes depends on its location, size and type. A scar may fade so much that one can barely see it, but it never completely goes away. Some scars cause problems months or years later. In such cases, the use of corticosteroids can be used to manage scars or out growth on the healing sight. The hormone corticosteroids increase basic fibroblast growth factor production while decreasing transforming growth factor-beta1 production by human dermal fibroblasts, endogenous vascular endothelial growth factor, and insulin-like growth factor [29,30].

It is normal to get wound in one's lifetime and except under two conditions for example wound in embryonic stage and the other is in the oral cavity, and get some out growth in and around the healed area. It is clear from the conditions when the wound is not exposed to the outer environment, it heals scar lessly. Therefore, it may be conjectured that some environmental factors may be responsible for scar formation during healing. Alternatively, some unknown factors are present in oral and uterine cavities, which inhibit scar formation. The increase of estrogen and estrogen/progesterone ratio in amniotic fluid may be also related to scar less wound healing, But then what about oral cavity? From the literature it was found that at least a few studies have reported [31, 32] the presence of estrogens receptors that are able to stimulate proliferation of basal epithelial cells and differentiation and synthesis of collagens. Thus estrogens clearly play a crucial role in both the physiology and pathology of oral epithelium. It is therefore highly likely that estrogens play a crucial role in scar free healing of wounds, Moreover as mentioned corticosteroids to manage keloids [33, 34], there is a possibility that estrogen may be better than corticosteroids

since they partially share the receptor [35]. It is also worth mentioning here that at least a few authors have mentioned the presence of different types of keratins in adult and fetal wounds and our group has established the role of estrogens in proliferation and genomic action on synthesis of types of keratins [36-40]. However further extensive experimental work is needed to prove this hypothesis.

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