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## **Dermatology** | Review Article

# The relationship between age and skin healing

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#### ABSTRACT

Proportion of elderly individuals in the population has increased, consequently, practitioners are often confronted to wound healing in elderly patients. The objective of this article is to approach skin aging and its consequences on skin healing, disorders of skin healing due to dermatoporosis and finally, specific comorbidities of the elderly that can cause wound healing perturbations. Considering these specificities, skin healing in the elderly is complicated and require a multidisciplinary management.

Keywords - comorbiditie; dermatoporosis; malnutrition; skin aging; skin healing

## **INTRODUCTION**

Skin healing in the elderly has many specificities that should be taken into account. Skin healing problems are, for instance, the direct consequence of skin aging, age related abnormalities, physiological skin healing process and general factors linked to the comorbidities observed in the elderly.

#### Skin aging and dermatoporosis

Skin aging manifests, over the years, through alterations in the skin lining, which consequently loses a part of its physiological role as a barrier. It is the consequence of intrinsic (genetically programmed) and extrinsic factors. Extrinsic factors are numerous, they include drug factors, which worsen the physiological xerosis (oral hypolipemiants, allopurinol, hydroxyurea and cimetidine) [1], deficits in essential fatty acids, vitamins, (vitamins group B, E, PP, C, A), zinc and magnesium and also the frequent states of protein energy malnutrition in the sick elderly person and the environmental factors such as smoking and exposure to ultraviolet light (UV) [2].



Clinically, skin aging causes xerosis, linked to the decrease of hydration of the stratum corneum, with a rough skin to the touch. Its frequency is estimated between 55% and 75% in subjects over 65 years old [3-4]. The xerosis is responsible for pruritus that should be properly managed, as it may limit compliance for compression bandages. This xerosis is associated with the decline of skin barrier function, sensory perceptions, sweat and sebaceous secretions and immunological and thermoregulatory functions [5].

On a microscopic scale, skin aging is manifested by a thinning in the dermo-epidermal junction, and an elongation in keratinocytes time renewal. In the dermis, we notice a decrease in the number of fibroblasts and therefore in the density of collagen fibers, elastic fibers and glycosaminoglycans, with a thinning of the dermal thickness. With the quantitative decrease is associated a qualitative decrease in residual fibers with a loss of trophicity and skin elasticity. During aging, a decrease in the hydrophilicity of glycosaminoglycans is thus observed. This chemical modification may explain the dermal thinning and the xerosis of the elderly subject, since glycosaminoglycans are responsible for hydration of the dermis.

Proteoglycans support the hydration of the extracellular matrix (ECM) of normal skin, providing resilience, viscoelasticity, and a cushioned environment conducive to cellular function and development. Proteoglycans are a multifunctional diverse group of matrix and cell-associated proteins each with a distinct localization in skin. Versican, together with hyaluronan, a variable molecular weight nonsulfated linear glycosaminoglycan, forms macro-aggregates that are important for skin hydration and viscoelasticity. Highly hydrated versican-HA aggregates yield looser matrices than aggrecan-HA aggregates and are hence more conducive to cellular migration, an important property for wound healing. Versican is a major component of blood vessels in skin and associated with elastic networks through G3-mediated interactions with fibulin -1 a component of elastic microfibrils. As with aggrecan, the lectin domain within the G3 region of versican also has the ability to interact with tenascins and matrilin-1 and -3, enabling stabilization of extended collagen-HA-versican networks within tissues. These networks are presumed to be important for sensing of the mechanical microenvironment at the local level, allowing these mechanosensory processes to regulate tissue metabolism. Proteoglycans can interact with other matrix molecules such as collagen to form and stabilize the ECM, thus producing the hydrated integrated structures required for responsive cells in a healthy intact skin.

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Cutaneous aging leads in the extreme to the phenomenon of dermatoporosis. The term dermatoporosis, by analogy with osteoporosis, was proposed by professor Saurat to define all the manifestations linked to skin aging leading to skin fragility and insufficiency (figure 1) [6]. Patients with dermatoporosis have, regardless of delay of healing, an increased risk of wounds due to skin atrophy (skin tears) and to risk of dissecting hematoma (figure 1) [7].





Figure 1: Skin fragility, skin tear and Bateman's purpura

## Consequences of age on scarring phenomena

Physiological wound healing has three stages directly impacted by aging: the first stage is hemostasis and inflammation, the second is cell proliferation and the third is tissue remodeling. As we age, platelet adhesion to the damaged endothelium is increased, slowing skin healing. The local inflammatory response to the wound is diminished as a result of decreased expression of adhesion molecules. The proliferation stage is also altered by the slowdown of keratinocyte renewal mentioned above, and also by a reduced response to growth factors. Finally, tissue remodeling, the final stage of healing, is also altered in the elderly due to an imbalance between metalloproteinases and their physiological inhibitors, in favor of metalloproteinases and thus the destruction of collagen [8]. The different phases of healing are therefore altered by these phenomena in the elderly: decreased bank contraction, cell proliferation, neovascularization, delayed inflammatory phase and slower epithelialization [9]. Apart from these deleterious aspects, skin healing in the elderly has certain advantages. Due to a less important inflammatory reaction, pathological scarring phenomena such as hypertrophic and/or keloid scars are rarely observed.

Moreover, in the case of skin resection, particularly for carcinoma, with sometimes significant loss of substance, the laxity of the skin of the elderly subject generally allows easy suturing, without tension, with a satisfactory aesthetic result. However, suturing can be difficult because of the risk of tearing increased by dermatoporosis.

## Frequent comorbidities in the elderly affecting wound healing

Numerous co-morbidities, affecting more particularly elderly subjects, alter the healing process. Undernutrition is a major factor in delayed healing. It is common in the geriatric patient and, associated with prolonged immobilization, leads to a major risk of sores formation.

Arterial insufficiency, frequent in the elderly, especially diabetics, delays the healing of heel sores and all distal wounds of the lower limbs. The ankle-brachial pressure index (ABPI) is essential in case of any lower extremity wound to assess arterial vascular status. In case of decreased ABPI (less than 0.9), additional vascular explorations should be carried out, as healing cannot take place correctly in the case of peripheral arterial occlusive disease.

Venous insufficiency often complicates the healing of a leg wound or angiodermatitis. The clinician should systematically raise the question of the indication for venous contention in the case of wounds of the lower limbs.

Cardiac insufficiency, responsible for edema of the declining zones, but also renal and hepatic edema, often limits the healing of wounds on the lower limbs. The wounds are then often oozing, with a strong tendency to maceration, particularly of the periwound skin due to saturation of the dressings. Management of the underlying pathology is then essential, with hydro-sodium depletion if necessary, combined with the application of highly absorbent dressings.



In the management of cardiac insufficient three different dialytic methods are used (UFI: ultrafiltration isolate; HF: hemofiltration; CAVH: continuous arteriovenous hemofiltration). These methods are used to cause a good depletion in the patients with intractable heart failure following from ischaemic valvular or primitive cardiomiopathy. The methods (HF and CAVH) that have depletive and depurative effects. Each of these methods is capable, without important differences, of achieving the following aim: the hydro-sodium depletion, and the correction of the haemodynamic alteration.

Discharging heel or forefoot wounds and splinting of wounds exposing a tendon is often essential for good healing. However, the benefit of discharge or immobilization in the elderly subject must be balanced by the risk that they entail: loss of autonomy, effort maladjustment, amyotrophy, getriatric cachexia. In addition, discharge shoes, such as Barouk, cause an imbalance in walking and increase the risk of falling often pre-existing in the elderly.

Cognitive disorders also limit wound management in the elderly. They represent a real challenge for the doctor and the caretaker, often making it difficult to apply dressings, to ensure proper detorsion, and of course to hold the dressings in place, as the patient with dementia often has a tendency to manipulate them.

Elderly patients are more exposed to treatments that may delay skin healing, particularly systemic corti- costeroid therapy and chemotherapy. Corticosteroids slow down the healing process through their anti-inflammatory action and the reduction of fibroblast synthesis. Chemotherapies have a direct deleterious role on wound healing by reducing cell migration and proliferation, as well as angiogenesis. Hydroxyurea (Hydrea\*), used in chronic hemopathies, can provoke ulcers but also slows down their healing (figure 2),. Because of the risk of hemorrhage, anticoagulants can also delay the healing process, making mechanical detorsion in particular more complicated.

Finally, ageing is associated with hormonal disorders, in particular a decrease in the level of oestrogen and its precursor, dehydroepiandrosterone (DHEA\*). These hormones play an important role in wound healing by promoting the synthesis of the extracellular matrix.



Figure 2: Hydrea<sup>®</sup> ulcer in an elderly person being treated for essential thrombocythemia [10]

## **CONCLUSION**

Scarring in the elderly is influenced by multiple factors. Wound healing disorders in this population are not seen in healthy elderly patients, but occur frequently and are directly related to the comorbidities which are common in this population, particularly undernutrition, venous insufficiency, arterial insufficiency and polymedication. When faced with a wound in the elderly, factors that may limit wound healing should be specifically assessed and managed.



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