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Review

Anatomy and Physiology of Wound Healing

Vigneshwaran. L V, Kathirvel. B*, Abinayah. S, Jeeva. S, Vasanth. S, Sivashankar. B, Jagatheeswaran. M

RKP College of Pharmacy, Krishnagiri, Tamilnadu, India.

*Author for Correspondence: Prof. Kathirvel.B
Email: kathirvel9443@gmail.com

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Abstract

To ensure the restoration of the integrity and function of the skin, a sequence of carefully orchestrated steps are engaged in the multifaceted process of cutaneous wound healing. Most importantly, the function of lipids in wound healing is explored with focus on how they augment restoration of barrier function, modulate inflammation, induce cell proliferation, and promote remodeling. Lipids including phospholipids, sphingolipids, and ceramides are required for membrane structure, cell signal, and tissue repair. Normal wound healing occurs in three successive but overlapping phases: the remodeling phase, the proliferative phase, and the hemostasis/inflammatory phase. Hypertrophic scar and keloid wounds are examples of wound healing abnormalities that compromise normal physical function.

Keywords: Wound healing, skin physiology, epidermis, dermis, hypodermis, inflammation, proliferation, remodeling, scar formation.

1. INTRODUCTION

To delve deeper into the intricate world of cutaneous wound healing, one must have a basic understanding of the structure and function of the skin. The skin, the largest organ in the human body, is composed of three main layers: the epidermis, dermis, and hypodermis (subcutaneous tissue). Each layer plays a distinct role in maintaining the skin's integrity.and when combined, they support the skin's general functionality, including its capacity to heal wounds. The three are the subcutaneous tissue, dermis, and epidermis highly vascularized and innervated multihistological layers that make up the skin. The first is distinguished by particular cell populations

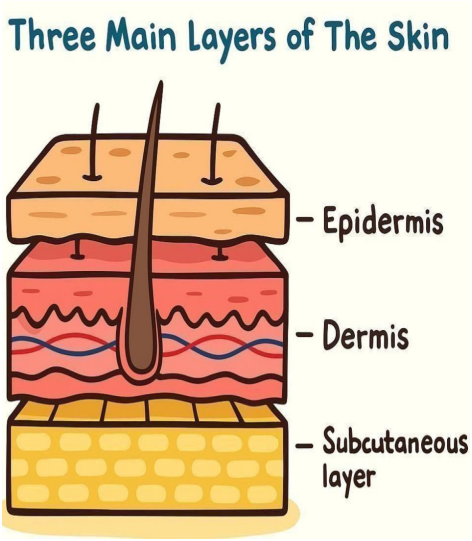
(such as melanocytes and keratinocytes) that are kept apart by the dermis by the epidermaldermal basement membrane. [1,2]

2. Skin

The extracellular matrix (ECM), a non-cellular substance that gives cells chemical and physical support and for intercellular connections and cellular proliferation, is prevalent in the dermis. Fibroblasts, fibrocytes, mast cells, and the structural cells of blood and lymph vessels are the cells that primarily make up the dermis. Additionally, the skin is abundant in skin adjuncts, such as glands and hair, which extend from the deeper dermis to the epidermis' surface. Melanocytes, Langerhans cells, and Merkel cells are also found in the epidermis, despite keratinocytes making up 90–95% of the cells there.

The epidermis is attached to the dermis by the basement membrane, a thin layer of glycoproteins made primarily of laminin and type IV collagen. Such anchoring is carried out by hemidesmosomes, which physically anchor basal epidermal cells to the subjacent dermis, and type VII collagen anchoring fibrils, which anchor the cytoskeleton in a vertical direction. The reticular and papillary dermis are the two areas that make up the dermal compartment. This compartment, which makes up the majority of the skin, is formed by thick, fibroelastic connective tissue.

The epidermis invaginates into the underlying connective tissue in the form of rete ridges or pegs.(1,2)



3.Anatomy and physiology of the skin

3.1: EPIDERMIS

The tissue known as stratified epithelium makes up the majority of the epidermis. One or more cell layers make up stratified epithelium. Since the epithelium always has a single free surface, no additional cells can stick to it. A basement membrane is the epithelium's opposing surface. This noncellular layer, which sits between the epithelium and the underlying connective tissue, is abundant in proteins and polysaccharides. As a result of continuous and fast cell division, which creates new cells beneath them, the cells that originate in the epidermis are forced towards its free surface. Keratinocytes constitute the majority of the epidermis' cells. Each is a little factory that produces the hard, water in soluble protein keratin. When these cells get to the mid-epidermal areas, they begin to make keratin.

There are five layers in the epidermis (10)

The horny layer, or stratum corneum

- Stratum lucidum, or the transparent layer
- Granular layer, or stratum granulosum
- The stratum spinosum (layer of prickle cells)
- Basal layer, or stratum basale

Stratum corneum

This is the epidermis' toughest, waterproof outermost layer. Dead cells that are fibrous and contain keratin make up the stratum corneum. Because the dead cells can withstand certain chemicals as well as pH and

temperature changes, they help the skin maintain its protective function. Every day, millions of cells are lost, yet new ones are constantly being produced via cell divisions. In the aftermath of trauma, this helps the skin heal itself. Additionally, because keratin can absorb water, prolonged exposure to an overly moist environment— such as urine or wound exudate may cause skin maceration.

Stratum lucidum

Particularly in regions of the body where the skin is thinner, this transparent layer of additional protection. Granulosum stratum the layer where keratinocytes lose their nuclei and start to flatten and die is called the stratum granulosum.

Stratum granulosum

The stratum granulosum Keratinization begins in the stratum granulosum, the layer where keratinocytes lose their nuclei and start to flatten and die.

Spinosum stratum

The stratum spinosum is situated above the basal layer. Desmosomes are spiny structures seen in live cells in this layer of the epidermis. These aid in preserving the epidermis' integrity.

Stratum basale

Also referred to as the basement membrane, this is the lowest layer of the epidermis. The stratum basale, which separates the dermis from the epidermis, is one cell thick. Skin renewal is made possible by the continuing division of the basal cells that comprise the **stratum basale.**

Active cell division gradually propels the daughter cells into the other layers of the epidermis, where they go through several phases of development. As the epidermis lacks a blood supply of its own, the stratum basale also regulates the flow of oxygen and essential proteins between the dermis and epidermis. With fibrils that extend into the dermis, the stratum basale also supports the epidermis.

3.2 Dermis

The main role of the dermis is to support and nourish the epidermis. The two layers recognized in the dermis are the papillary layer and the reticular layer. The papillary layer, or stratum papillare, is the dermal layer that lies closest to the epidermis, which is demarcated by a wavy boundary from the epidermis. This wavy shape enhances contact with thevepidermis, and provides that the dermal blood vessels are able to best nourish the stratum basale of the epidermis.

The papillary layer contains loose connective tissue, capillaries, elastic fibres, reticular fibres and collagen. The more substantial, reticular layer, or stratum reticulare, has denser connective tissue, larger blood vessels, elastic fibres, and collagen bundles in layers. Its chief component is the proteinaceous connective tissue consisting of arc-shaped elastic fibres and undulated, very nearly inelastic, collagen fibres.

These impart to the dermis its high elasticity and tensile strength, and repel injury from daytoday stretching and other mechanical assaults. Glycosaminoglycans (also referred to as mucopolysaccharides) link to proteinaceous connective tissue to create proteoglycans.

These create a gel-like mass that is able to absorb and release water just like a sponge. Some of the other ingredients of the dermis include several types of cells like fibroblasts, mast cells and other tissue cells, and numerous blood and lymph vessels, nerve endings, hot and cold receptors, and tactile sensory organs.

3.3 Hypodermis

The hypodermis (also known as the superficial fascia), is a tissue that anchors the skin while allowing some freedom of movement. It provides support for the dermis and is made up of largely adipose tissue, connective tissue, and blood vessels. Fat stored in the hypodermis helps to protect internal structures and also provides insulation against cold.

4. Functions of the skin (10)

4.1: Protection

The skin is the primary barrier that keeps interior tissues safe from harm caused by toxins, bacteria, temperature fluctuations, ultraviolet (UV) light, and physical trauma. It also regulates the loss of essential chemicals and keeps dangerous compounds out of the body.

4.2: Sensation

The body can sense changes in temperature, pressure, touch, and pain thanks to the nerve endings in the skin. The skin's nerve endings enable the body to sense pressure, touch, temperature changes, and pain.

4.3: Thermoregulation

The process by which the skin's blood vessels dilate or contract in response to temperature variations. Sweat is produced by the sweat glands and remains on the skin, allowing the body to cool. The erector pili of the hair contract when the body is chilly, lifting the hair and trapping warm air near the skin.

Extraction from the skin

Sweat, which comprises water, urea, and albumin, is the excretory function of the skin. The sebaceous glands release sebum, an oily material that lubricates and shields the skin. Metabolism: Vitamin D, which is necessary for calcium absorption, is produced by the skin in response to UV light. Nonverbal communication: blushing and other color changes in the skin can be used to express mood swings.

5. Wound

A wound is a break in the skin that might be caused by a medical or physiological condition, or it can be caused by mechanical, physical, or chemical assault. For instance: Trauma to the body: pressure sores Abrasions, cuts, grazes, surgical knife wounds, gunshot wounds, bites, etc. are examples of mechanical trauma. Heat trauma includes frostbite and burns caused by heat, chemicals, radiation, friction, or electricity. Medical or physiological conditions include autoimmune diseases, endocrine disorders, dermatology, hematology, and arterial or venous ulcers. brought on by some systemic infections, cancerous diseases, or neuropathy.

6. CATEGORY OF WOUND HEALING (9)

6.1 Category 1

Primary wound healing, or healing by first intention, takes place within hours of the closure of an intact full-thickness surgical incision. This surgical trauma leads to the death of a few cellular components.

6.2 Category 2

If the wound margins are not approximated immediately, delayed primary wound healing occurs. Such healing is favored in the context of contaminated wounds. By the fourth day, phagocytosis of infected tissue is in full swing, and epithelization, collagen deposition, and maturation are underway. Foreign substances are isolated by macrophages that can transform into epithelioid cells, which are ringed by mononuclear leukocytes to form granulomas. The wound is generally closed surgically at this point, and if the "cleansing" of the wound is not complete, chronic inflammation may follow and produce obvious
scarring.

6.3 Category 3

A third form of healing is called secondary healing, or healing by secondary intention. For this form of healing, a full-thickness wound is permitted to close and heal. Secondary healing yields an inflammatory response that is greater than with primary wound healing. Also, a greater amount of granulomatous tissue is synthesized due to the necessity of wound closure. Secondary healing produces severe wound contraction. Fibroblastic conversion into myofibroblasts, which are contractile smooth muscle-like, is thought to be responsible for contraction of the wound. Myofibroblasts are found in maximum numbers in the wound between the 10th-21st days.

6.4 Category 4

Epithelialization is the migration and multiplication of epithelial cells by mitosis and penetration through the wound. This is part of the wound healing phases described in Sequence of Events in Wound Healing. In partial thickness wounds that only affect the epidermis and superficial dermis, epithelization is the most common way healing takes place. Wound contracture is not a feature of this process if only the epidermis or epidermis and superficial dermis are affected.

7. General classification of wounds and burn wounds. [8]

OPEN WOUNDS	CLOSE WOUNS
Incision Laceration Contusion bruises Abrasion Ulceration Burn Wounds Bite sting Wound Abscesses	Contusion bruises Crush wound Blister Seroma Hematoma Tumor

8.Physiologic Skin Wound Healing

8.1Wound Healing

`[1] Wound healing is characterized by an ordered sequence of overlapping phases that culminate in tissue reconstitution. This process includes the following steps: hemostasis, inflammation, proliferation, and the formation of mature scar tissue.(10) The physiology of wound healing can be complicated. Numerous internal and external factors might have an impact on the wound healing process. Therefore, it is crucial to collect a complete patient history and diagnose any underlying disorders that may affect healing while treating a patient who has a wound. Restoring the injured area to normal strength and function or as close to normal as possible is the primary goal of the wound healing process. However, increasing a patient's quality of life will be the ultimate goal for

some patients with wounds, especially in palliative care settings, rather than wound healing. Acute and chronic wounds are frequently separated, and they might heal with main or secondary aim. [3] Skin tries to repair itself when it is injured in order to keep protecting the body. Animal models used in research on acute wounds reveal that wounds heal in four stages,

- Hemostasis
- Inflammation
- Proliferation
- Maturation

8.2 Hemostasis

[1] Hemostasis corresponds with the time of the injury, and the processes used to control bleeding from the wound include vascular constriction, platelet thrombus formation, prolongation of the coagulation cascade, clot termination, and fibrinolysis. The initial phase of wound healing, also known as the pro-inflammatory phase, begins during the course of injury and lasts for a few hours.

The main objectives of this phase are hemostasis and the formation of a temporary wound matrix.[4] The temporary measures offer protection from invasion by infection and from further bleeding [6] Platelets in the plug release growth factors and cytokines, such as insulin growth factor (IGF), transforming growth factor-{(TGF-}), PDGF, and epidermal growth factor (EGF), which are essential cellular mediators for the subsequent phases of healing. The release of platelet factors is most intense during the first hour of platelet activation, but it can last for up to seven days. Other cell types in the wound, including fibroblasts, monocytes, endothelial cells, and smooth muscle cells, are paracrinely impacted by these factors.

Due to the high concentration of growth factors released by activated platelets, platelet-rich plasma (PRP) has been successfully tested in both small and large animal models for the treatment of a variety of injuries, including wounds.

It is also referred to as the pro-inflammatory stage and begins following injury. At this point, tissue damage causes the damaged tissue to release prostaglandin 2-α and thromboxane A2 into the wound bed. This triggers a potent vasoconstrictor response, which causes the tiny blood vessels inside the wound to constrict and cause hemostasis.

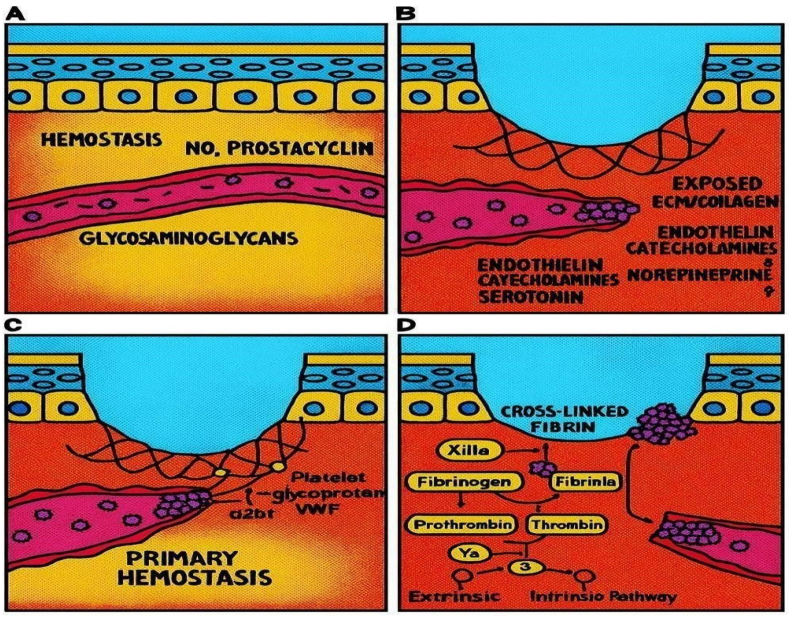
[2] After 5 to 10 minutes of vasoconstriction, blood vessel dilatation, or vasodilation, occurs, peaking about 20 minutes after the injury. the end result of platelet-derived growth factor [PDGF], serotonin, fibronectin, fibrinogen, histamine, platelet-released growth factor [EGF], and Von Willebrand factor, among other cell factors. Platelet aggregation, degranulation, and coagulation cascade activation are the outcomes of the interaction between platelets and subendothelial collagen.

Vasocontraction

[6,5] Blood flows to the wound site when the vascular endothelium is damaged, exposing the basal lamina. After activated platelets attach to the exposed collagen, a variety of growth factors, inflammatory mediators, and cytokines are released. In order to stop additional blood loss, a fibrin clot forms a seal and the intrinsic and extrinsic coagulation pathways are triggered.

Vasoconstriction Vessels quickly constrict after damage to stop bleeding from ruptured microvasculature. Vasoconstrictors like endothelin, which are released from the injured endothelium, cause the vascular smooth muscle to contract reflexively, achieving this. Vasoconstriction is also controlled by circulating catecholamines, norepinephrine, epinephrine, and prosta-glandins that are released from damaged cells. Platelets generate PDGF, a substance that preferentially activates mesenchymal cells, particularly smooth muscles in the vessel walls, resulting in contraction.

However, bleeding is only momentarily reduced by initial reexive contraction. This is because the wound's growing hypoxia and acidosis cause the muscle to passively relax, which restarts the bleeding. To further control vasoconstriction through the mediators bradykinin, fibrinopeptide, serotonin, and thromboxane and permanently stop bleeding, the coagulation cascade must be activated later.



A. Cellular reactions during the wound-hemostasis stage. A: Platelets move in close proximity to the vessel wall during hemostasis. However, endothelial cells release antithrombotic substances like prostacyclin and nitric oxide (NO), which stop platelets from adhering to the endothelium lining and from aggregating.
B. Wounding causes damaged cells to release vasoconstrictors quickly, which results in smooth muscle reflexive contracture and a brief halt to bleeding.
C. The subendothelial matrix is exposed when blood vessels burst during wound healing. G protein-coupled receptors, integrins, and glycoproteins on the surface of platelets allow them to attach to this subendothelial matrix and to one another. Additionally, platelets release von Willebrand factor (vWF), which adheres to the subendothelial matrix. Through their surface receptors, platelets bind extracellular vWF, fortifying the platelet plug.
D. Both intrinsic and extrinsic pathways cause Factor X to become activated, which in turn causes fibrinogen to be cleaved into fibrin. The aggregated platelet plug is bound by crosslinked fibrin to form a thrombus, which halts blood flow and supplies a temporary healing matrix. The image is a simplified representation based on what is currently understood.

8.3 Inflammation

[1,2,4] The inflammatory phase of the wound healing cascade, which is clinically referred to as the debridement phase, is initiated during the hemostasis/coagulation phase. In the early days following an injury, inflammatory cells migrate to the wound site after platelet activation. Mast cells release vasoactive cytokines, such as prostaglandins and histamine, to promote migration. These cytokines increase capillary permeability and promote local dilatation. Pattern recognition receptors on tissue-resident macrophages in the dermis are activated after an injury by pathogen-associated molecular patterns on pathogens and danger associated molecular patterns released by necrotic and damaged cells.

Inflammatory cells migrate to the wound site as a result of increased blood flow and vascular permeability. Complement C3 is activated by the presence of foreign organisms, and the bacterial lysis is the result of a series of nonenzymatic protein cleavages and interactions. Neutrophils are then drawn to the wound site as a second responder cell as a result of tissue damage that causes the production of cytokines and other inflammatory mediators. These cells are in charge of complement-mediated opsonization, debris scavenging, bacterial death through oxidative burst processes, and the engulfment and lysis of invading organisms. The waste products produced by neutrophil activity were either ejected with eschar or phagocytosed by macrophages.

Neutrophils are attracted to the wound site during the first twenty-four hours and remain there for two to five days. Neutrophils are the most common cells at the wound site during the early stages of inflammation. Macrophages carry out phagocytosis after neutrophils initiate it. By releasing ROS, nitric oxide (NO), and proteases, these phagocytic cells remove local pathogens and debride necrotic tissues. Neutrophils can also eliminate pathogens in the extracellular environment by employing neutrophil extracellular traps, which are weblike structures composed of strands of decondensed chromatin connected to bactericidal proteins produced by neutrophils.

The wound site attracts neutrophils. During the first twenty-four hours and remain there for two to five days. Neutrophils are the most common cells at the wound site during the early stages of inflammation. Macrophages carry out phagocytosis once neutrophils initiate it. By releasing ROS, nitric oxide (NO), and proteases, these phagocytic cells remove local pathogens and debride necrotic tissues. By using neutrophil extracellular traps, which are weblike structures made of strands of decondensed chromatin connected to bactericidal proteins produced by neutrophils, neutrophils can also eradicate pathogens in the extracellular environment.

Neutrophils' function in wound healing.

[5]A: Neutrophils are attracted to the wound as soon as resident cells release lipid mediators, calcium waves, hydrogen peroxide, chemokines, and damage-assocmolecular patterns (DAMPs).

B: Neutrophils combat infections by releasing proteases from their intracellular granules. They also produce neutrophil extracellular traps (NETs), which capture pathogens through a process called NETosis. Neutrophils extend chromatin filaments coated with proteases outside of the cell to aid in the removal of pathogens.

C: Neutrophils also perform phagocytosis in the wound. They produce a phagocytic cup that absorbs antigens and uses surface receptors and integrins to probe them. Internalized antigens are broken down by proteases in the neutrophil granules.

D: The timely elimination of neutrophils is essential for the resolution of inflammation. They can either be engulfed by macrophages through efferocytosis or re-enter the circulation and leave the wound through a process called reverse migration. The picture is a simplified depiction of what is currently known.

[2] **Macrophages**

Are crucial to every step of the wound healing process and coordinate it all. During the early inflammatory phase, macrophages carry out pro-inflammatory functions such as phagocytosis, antigen presentation, and the production of growth factors and inflammatory cytokines that aid in wound healing. Wound macrophages most likely display the classically activated, or "M1 phenotype," phenotype at this point.

In order to fully form the extracellular matrix (ECM), angiogenesis, and epithelialization, macrophages later promote the proliferation of skin, endothelial, and epithelial tissue during the proliferative phase of healing. During the remodeling stage, macrophages can change the composition of the extracellular matrix by releasing degradative enzymes**.**

This implies that alternatively activated macrophages, or the "M2 phenotype," play a significant part in this stage of wound healing. Severe heat damage also results in immunosuppression due to seriously damaged lymphocytes. In the end, burned tissue's cellular reaction aids in phagocytosis and removes toxins and dead tissue from the wound site.

Macrophage phenotypes in wound healing

[5] A: Bone marrow-derived circulating monocytes continuously roll over the inner endothelial wall in the vessel lumen of the uninjured skin, looking for damage. The perivascular space is home to a small number of skin-resident macrophages, some of which may have embryonic origins.

B: During the inflammatory phase of skin damage healing, macrophages release proinflammatory cytokines such as interleukin (IL)-6, tumor necrosis factor (TNF)-~, and IL-1 to combat infection. Early macrophages in the wound release monocyte chemoattractant protein (MCP)-1 to draw in additional monocytes from the bone marrow and boost the macrophage response. These macrophages also actively participate in the phagocytosis of pathogens. The inflammatory stage of wound healing ends when neutrophils are ingested by macrophages.

C: Macrophages release growth factors such as vascular endothelial growthfactor (VEGF) and platelet-derived growth factor (PDGF) as granulation tissue grows during the growth stage of wound healing. These factors are used to signal and activate endothelial cells to perform angiogenesis. At this point, some macrophages release extracellular matrix (ECM). Fibrosis can result from uncontrolled ECM deposition, and these scar-forming macrophages are known as fibroblasts.

D: In order to restore homeostasis to the healed skin, macrophages once more assume a phagocytic function during wound remodeling, engulfing excess extracellular matrix and cell debris. The image is a simplified representation based on what is currently understood.

8.4 Proliferation

[1,5] The proliferative phase, also referred to as the repair phase in clinical settings, aims to protect the surface of the wound by forming granulation tissue and a new epithelial cover, as well as to restore the vascular network to support the developing tissues. When inflammation goes down, the proliferative phase begins, which

is characterized by the formation of granulation tissue, re-epithelization, and restoration of the vascular network. This phase begins four days after the injury and lasts for fourteen days. As the inflammation subsides, the body releases a range of cells, including those involved in migration and proliferation.

During the proliferation phase, the temporary wound matrix produced during hemostasis is replaced by granulation tissue, which is made up of multiple fibroblasts, granulocytes, macrophages, and blood vessels in complex with collagen bundles.

This partially restores the structure and functionality of the injured skin. Granulation tissue development depends on fibroblasts, which primarily migrate from the surrounding dermis to the wound in response to growth factors and cytokines produced by platelets and macrophages in the wound, including PDGF, transforming growth factor (TGF)b, and BFGF.

Mast cells in wound healing

[5] Their function in scar formation has been tested using a fetal wound healing model. The foundation of this model is the notion that mouse wounds at embryonic day 15 do not leave scars, but wounds at embryonic day 18 do. Interestingly, by injecting mast cell lysate into wounds at embryonic day 15, scarless healing can be converted to scar formation.

However, when mast cells are removed at embryonic day 18, there is less scarring. These studies show that mast cells play a role in the scar response, but they still need to characterize the exact mechanisms that underlie this process. The role of mast cells in chronic wounds has also not received enough attention.

This stage of wound healing is essentially the same for burn wounds and other types of wounds. The reepithelialization process is thus initiated within a few hours after injury by keratinocyte migration from viable skin appendages in the dermis (such as sweat glands and hair follicles). The extent and depth of the wounds still play a major role in this. In a first degree burn wound, the basement membrane remains intact, and epithelial cells migrate upward as usual.

The fibroblasts and pro-repair macrophages found in the granulation tissue influence the reepithelialization of keratinocytes. This process is initiated by the production of TGF-α, keratinocyte growth factor, and epidermal growth factor by platelets, keratinocytes, and activated pro-repair, anti-inflammatory macrophages. By producing fibronectin, tenascin C, and laminin 332, keratinocytes also initiate a feedback loop that activates fibroblasts.

Within three days of tissue damage, epithelial stem cells begin to proliferate from the basal layer of the epidermis and hair follicle root sheaths, while keratinocytes begin to migrate centrally from the wound's edges within hours. The keratinocytes travel along the wound's edge until they are in close proximity to one another. The inhibition of contact by the surrounding keratinocytes stops migration.

The new extracellular matrix needed for granulation tissue and vascular support is made by migrating fibroblasts producing collagen and elastin. Granulation tissue is a highly vascular connective tissue that is essential for the final stages of wound healing, maturation, and remodeling. The final stage of the proliferation phase is the development of granulation tissue. Fibroblasts migrate to the wound site and proliferate when macrophages and other immune cells generate growth factors. The existing fibrin clot is broken up by the MMPs that these fibroblasts produce. Fibroblasts then produce a transient matrix of collagen type III, glycosaminoglycans, and fibronectin.

This process replaces the fibrin clot with a new temporary matrix that promotes keratinocyte migration for reepithelization. The newly formed granulation tissue is composed of loosely arranged collagen bundles, capillaries, granulocytes, fibroblasts, and macrophages. This young tissue's inadequate angiogenesis gives it a traditional crimson look.

8.5 Maturation

[1,5] The maturation phase, the final stage of wound healing, includes collagen crosslinking, remodeling, and wound contraction. In healthy skin, type 1 collagen is more abundant and thicker than type 3 collagen, which is initially made by fibroblasts. Sweat glands, intact hair follicles, and the area surrounding the wound's edges contain epithelial cells. These cells migrate over the newly formed granulation tissue and contract, causing the wound to shrink and its edges to come together. When type 1 collagen replaces type 3 collagen in granulation tissue during the maturation phase, a scar forms.

This increase in type 1 collagen is linked to the improved strength of wounds seen 4-5 weeks after healing. A wound will regain 80% of its original strength three months after an accident. Unfortunately, it is hard to get the skin back to how strong it was before the injury.

The granulation tissue that develops following the injury is helped to contract by Myofibroblastic cells, which differentiate from fibroblasts in situ. Myofibroblasts regulate tissue remodeling and wound contraction by releasing extracellular matrix molecules and assuming a contractile phenotype, which is brought on by actin. The differentiation of fibroblasts into myofibroblasts appears to be regulated by the presence of TFGbeta1 in the skin

microenvironment and probably the same conditions of non-deformability of the extracellular matrix (ECM) regulated by molecular modifications (for instance, replacing collagen III with collagen I) that confer tensile strength. Only 80% of the skin's original tensile strength can be restored after severe damage, and some skin components, like sweat glands and hair follicles, cannot be restored.

In addition to the formation of new tissue, wound contraction begins during remodeling. TGFβ1 stimulates fibroblasts to become myofibroblasts. In addition to generating crucial extracellular matrix proteins such as collagen types I through VI and XVIII, glycoproteins, and proteoglycans, myofibroblasts also aid in wound contraction. Myofibroblasts are similar to smooth muscle cells, express α-smooth muscle actin, and can generate traction and strong contractile forces throughout the wound site. By aiding in the approximation of the wound's borders, this contraction promotes wound closure. Myofibroblasts die after the wound has fully epithelized.

Prolonged or severe myofibroblast activity can result in fibrosis and the formation of scars. A mature wound is mostly acellular, and fibroblastic cell apoptosis is a key factor in its development. However, our understanding of the apoptotic mechanisms underlying wound healing is still incomplete. Recent research suggests that these wound-bed myofibroblasts might differentiate further into fat cells to repair subcutaneous adipose tissue.

10. CONCLUSION

Wound healing is a dynamic and complex biological process involving a sequence of overlapping phases hemostasis, inflammation, proliferation, and maturation that collectively restore skin integrity and function. Proper coordination between cellular and molecular events is essential for effective tissue repair, while disturbances in these mechanisms may result in delayed healing or abnormal scarring such as hypertrophic scars and keloids. A clear understanding of the anatomy and physiology of skin, along with the cellular responses that drive wound repair, is vital for developing improved therapeutic interventions. Continued research in this field will support innovations in wound management strategies and enhance patient outcomes.

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