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REVIEW ARTICLE

Skin Wound Healing: An update on the Current knowledge and Concepts

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ABSTRACT:
Skin wound healing is a natural biological response to an injury. It is a complex process involving cellular activities. Tissue undergoes fibrotic reactions that result in the production of a scar. Tissue Engineering helps in curing major wounds. In case of chronic burns, stem cell skin is implanted. New tissue gets regenerated. Chronic wound can be healed by collagen. Bio-film acts a microbial reservoir for infection of neighboring tissue. Collagen has many great potential in medical uses. Blood borne oxygen is very much essential for healing and repairing process. Hemostasis phase, Inflammatory phase, Proliferative phase, Maturation phase are the stages of wound healing. Common wound can be cured by antiseptic ointments and dressings. Epidermis gets regenerated and grafting of skin develops over wounded area. However, these biological substitutes helps in restoring, maintaining and improved tissue functioning for healing factor.

KEYWORDS: Bio-film, tissue engineering, collagen, wound healing.

INTRODUCTION:
When a person is injured by burns, diabetic foot ulcer or any major wounds, artificial graft availability will be in major demand. A cultured keratinocyte (KC) is further used. The quality of scaffolds should be stable to achieve clinical outcomes[1]. Large amount of collagen is produced by scleroderma fibroblast[2]. Acetobacter xylinum is used for healing. The membrane never –dried nanostructure helps for faster healing. In order to deliver drugs to the chronic wound polymers such as collagen, chitosan is used. Proliferation leads to inflammatory response. Nutritional deficiency can delay the process of wound healing. Vitamin E, Vitamin C and Vitamin A plays a role on faster healing[3-6]. Dermo-epidermal substitute is for rapid vascularization[7]. To resist the contraction, tissue engineered skin of neo-vascularization is improved. Povidone- iodine acts as an antimicrobial agent which results in lacking of resistance development by bacteria. Natural bio-polymers used as artificial skin i.e; incase of lagging of availability of artificial skin. The foetal skin completes the regeneration of skin without scarring[8-10].

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Integra artificial skin:
Artificial integra is used in the surgery of chronic burns. Dermal regeneration template (Integra ^{TM}) is used to graft artificial donor into a normal epidermal components i.e; a normal functioning skin[11]. Cultured Epidermal Autograft (CEA) is used in some cases. Purpura fulminas results in extremity necrosis of the skin. So the need of extremity amputations will be more. Integra Artificial Skin is used for closure of wounds[12-14]. Autologous graft can be done for massive burn treatment. Rather than forming scar this replacement helps in regenerating the skin[15]. Integra provides the scaffold which is used for deep coverage of all wound defects[16]. Chitosan gelatin hyaluronic acid scaffolds exhibits viability. Dextran hydrogels offers opportunities in treatment of burn due to its soft and pliable nature. Release of natural polmers helps in reducing scar formation and healing wounds[17-19].

Phases of Wound Healing:

1. Haemostatis:
Cytokine production, phagocytosis is exerted in pro-inflammatory functions[20].

2. Inflammation:
Bacteria remains the same in inflammatory phase[21].

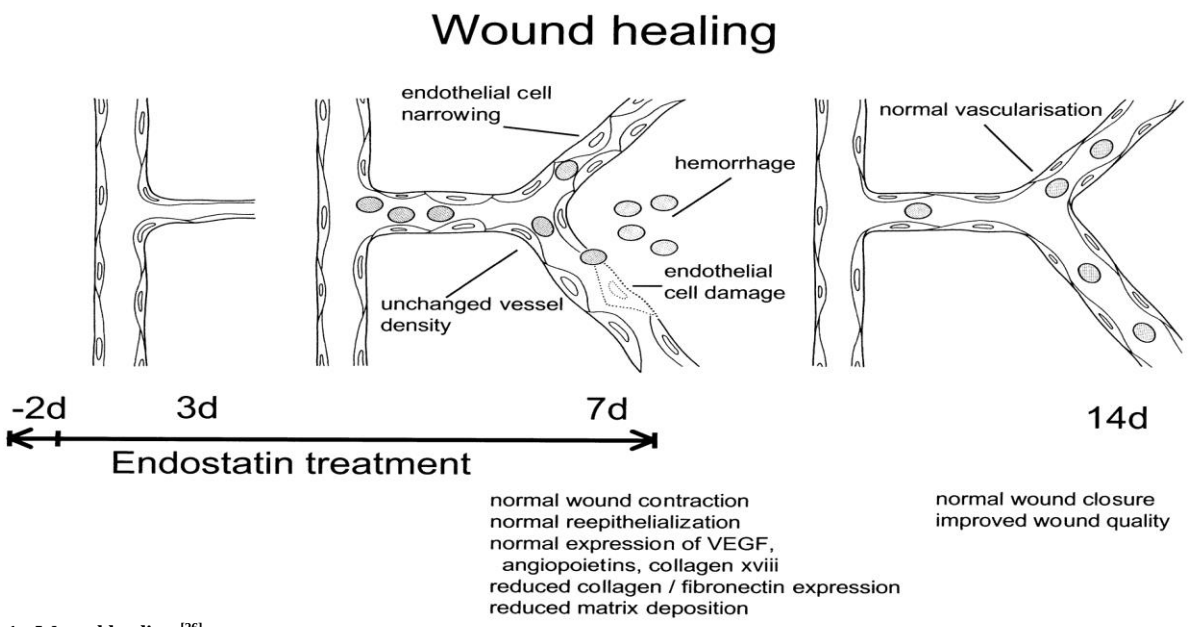

Fig 1: Wound healing [26]

3. Proliferation:

During this phase Vascular Endothelial Cell Growth Factor mediates a prolonged stimulus. Fibroblast growth factor supplies angiogenic stimulus. One of the essential component is Angiogenesis. Cutaneous wound healing take place in fibroblast activity[22, 23].

4. Wound healing:

For wound healing apoptosis is involved. Calcium is very much essential for wound healing. During macrophage process ECM, neo-vascularization and re-epithelialization complete its formation[20, 24-26].

Collagen:

The materials derived from collagen is used in wound healing[27]. It is a main protein of our skin. Collagen confers strength, stability to skin. Collagen fibril is the building block of collagen. Scaffolds based on collagen is useful for wound healing. Cell-to- matrix interaction helps in regulation of wound healing. In case of chronic burns the proteolytic reduction of plasmin, HLE, MMP -1,-2,-8,-9 takes place[28-30]. For skin regeneration materials based on protein delivery system will be useful for cell and as well as growth facto[19]. Engineering of natural polymers can be done for releasing the growth factor and its releasing factor[22]. For wound healing hyaluronic acid, fibronectin is helpful. Role of macromolecule is very much important for wound healing[31]. Decrease in the collagen gene transcription, mRNA levels and its production takes place in TNF Alpha[32]. Wound is covered by autologous split skin transplant where there is a chances of succeeding[33]. For repairing soft tissue, addressing of collagen materials which are in gel form, films and matrices have been addressed[34]. To prevent from further infection ColActivePlusAg is useful[35]. Glycolic acid used in clinical purpose due to the production of elevated collage [36]. Polyurethane dressing can improve healing the wounds[37].

Skin regeneration (tissue engineering):

For the completion of function, normal human tissue stimulates remodeling and angiogenesis. Skin graft method is very simple and safety method. Since acellular dermis retains the native dermis it is repopulated by host fibro-vascular cells[38,39-41]. For split-thickness of skin; calcium sodium alginate is used as a dressing[42]. Skin graft isogenic recepients is immunized and stimulates the immunity of transplantation[43]. Neo-angiogenesis is a mechanism for the integration of skin graft. Wound healing, tissue revascularization is promoted by Effect of Short Wave Therapy (ESWT)[44]. After the decellularization of alloderm, it is mixed with autologous skin for treating the chronic wounds[45].

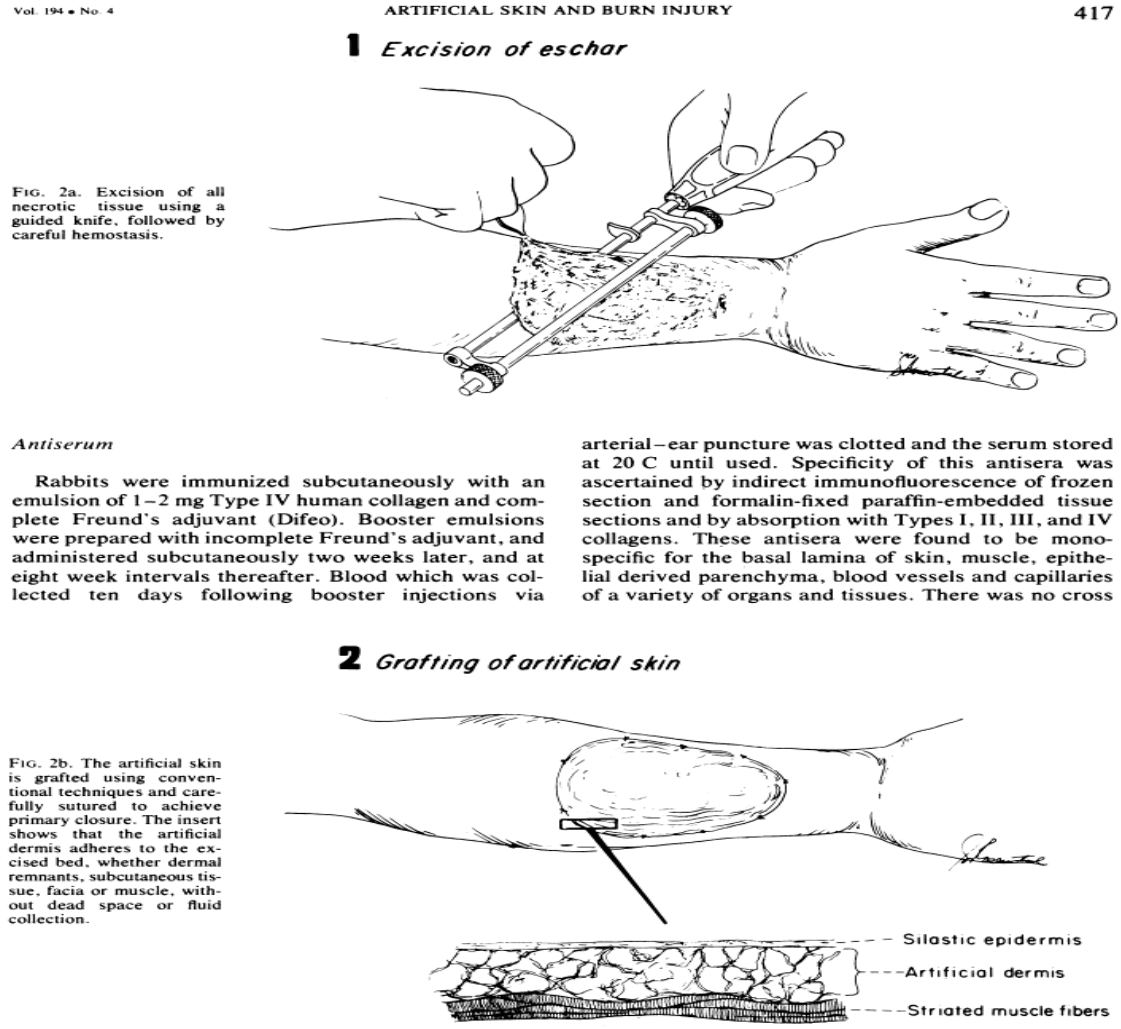

Fig 2: Grafting to skin and excision of eschar [38].

For temporary dressing xenograft, allograft is used. Accompanying of haemorrhage can be limited by using excision and grafting[46,47,38].

Silver stream:

Silver nanoparticles helps in rapid healing of wounds. By its antimicrobial property, it shows positive effect. When silver nanoparticles delivered to the skin, silver ions gets released and antimicrobial activity takes place. Thus providing an insight for therapy using silver nanoparticles[48-50].

Stem cell therapy:

Stem cells are used in curing chronic wounds[51]. Using some kind of cultured devices and enriched serum; expansion of mesenchymal stem cells occurs with no re-occurrence of inflammation. Healing of wound is a self-process. Contribution to wound healing is by stem cells [52,53]. For wound healing adipose derived stem cells is useful. Effect of Hypoxia results in synthesis of collagen, fibroblastic dermis and proliferation of ADSC's takes place for wound healing process[54].

Limitations:

Skin autograft, excision mostly fails to prevent the skin from necrosis process[52]. There is a lack of availability of autologous skin[13]. Factors affecting wound healing mechanism involves infections, diabetes, nutrition, stress , obesity ,medications and alcoholism .When wound healing does not attain anatomic and functional integrity then it leads to chronicity in wound[55,56].

Benefits:

In excision method loss of blood is minimum[46]. At present there are many advances in intensive clinical treatment[13]. Amniotic membrane helps in curing burns [57]. In wound dressing Ag\graphene composite hydrogel acts as a promisin applications. Integra acts an alternative skin grafting of full –thickness and it is readily available. Moreover integra covers the chronic

wounds. Prevention of wound dessication and healing the wound is enhanced by occlusive dressing[58-60]. In case of wide range of patients including diabetes; tissue engineered construct helps in curing both chronic and acute wounds. Without the production of scar wound can be healed by using biocompatible, resorbable extracellular matrix that can directly enlist to the injured site[61]. Metallic silver acts as an antimicrobial agent which develops resistance against antibiotics[62].

CONCLUSION:

In this era, more advancement is taking place in wound care. Dressing should be simple. There must be plan to care about all conditions of wound. Complication is about the expensive cost. As the range of wounds gets increased wound care becomes more complex. For further development of wound healing, maintenance of good sanitary water and hydrogels performing desired antibacterial action should be promoted. If there is some development in future which overcomes the limitations then definitely skin wound healing methods acts as one of the promising applications.

Future directions:

The future prospects of advancement will definitely result in gain. Skin grafting, tissue engineering, usage of silver ions, dressing the wound are the emerging techniques, in which each and every method is used based on its injuries. Though it is very helpful yet there are some limitations. Generally wound healing of large burns involves artificial skin replacement. Instead of undergoing replacement it's better to stream silver ions into the chronic wounds in upcoming years since it requires only antimicrobial activity and can be implicated for wound healing. The usage of Nano silver ions might result in conditions such as argyria due to its strong microbial agent. Finding out innovative materials and advanced technologies in Nano silver ions will show the signs of future success in skin wound healing**.**

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