THE UNIVERSITY OF JORDAN

Normal Wound Healing

Prepared by : Dr. Bareqa Salah

- Wound closure:

A. Primary closure: Immediate suturing of the wound
B. Delayed primary closure: Leave stitches in the wound and close it after 3-5 days when wound is clean. We do this method for contaminated wounds.
C. Secondary closure: By scar formation and epithelisation.
D. Tertiary: By graft or flap.

- Phase of Wound Healing: Look at the diagram

A. Inflammatory
B. Proliferative phase
C. Remodeling phase

Please refer to these links:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2903966/

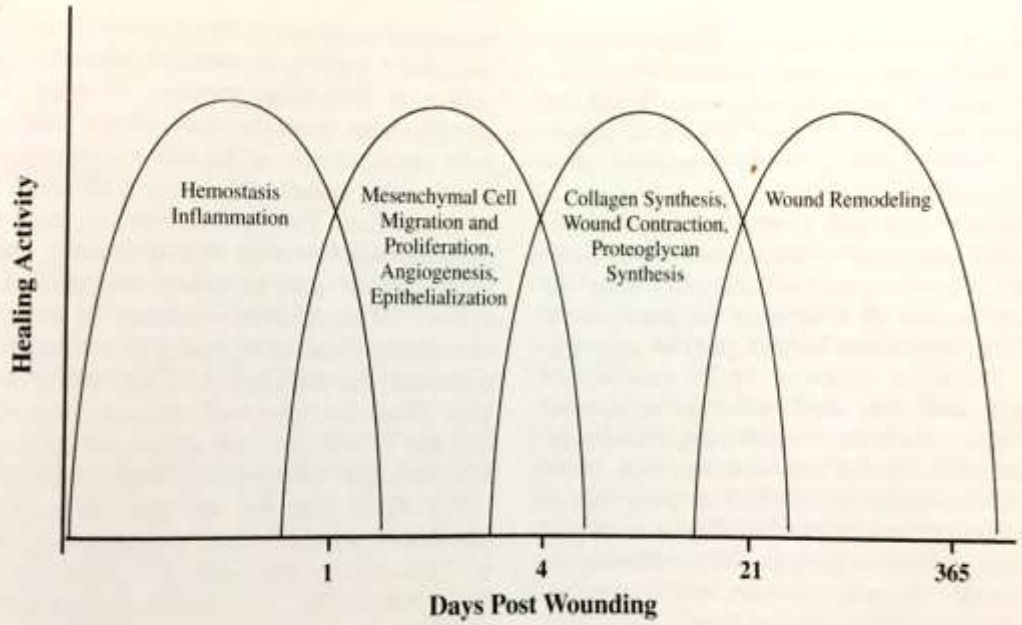


Figure 1. Phases of the healing process.

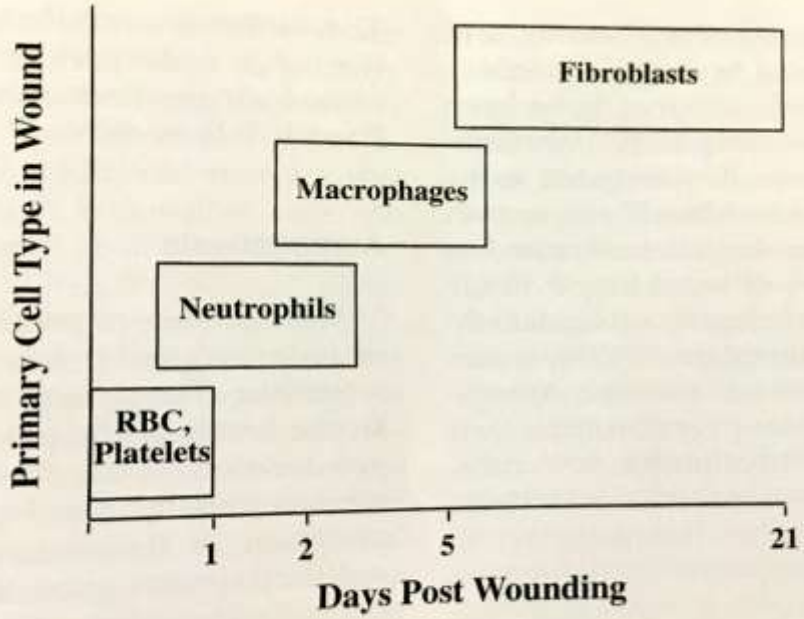


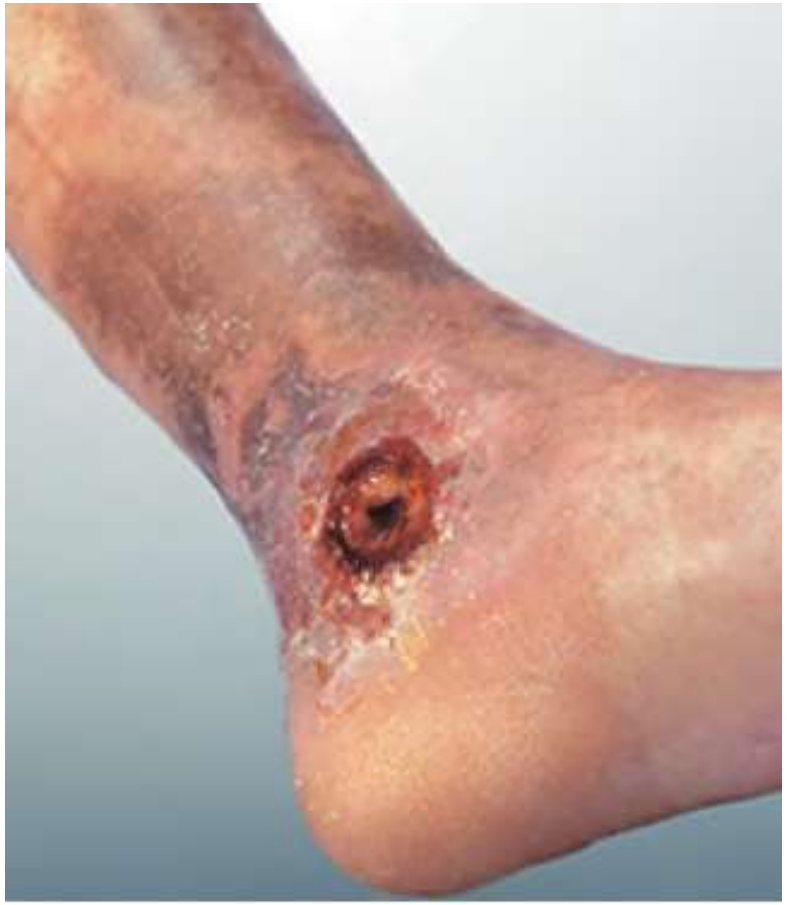
Figure 2. Cellular makeup of the healing wound.

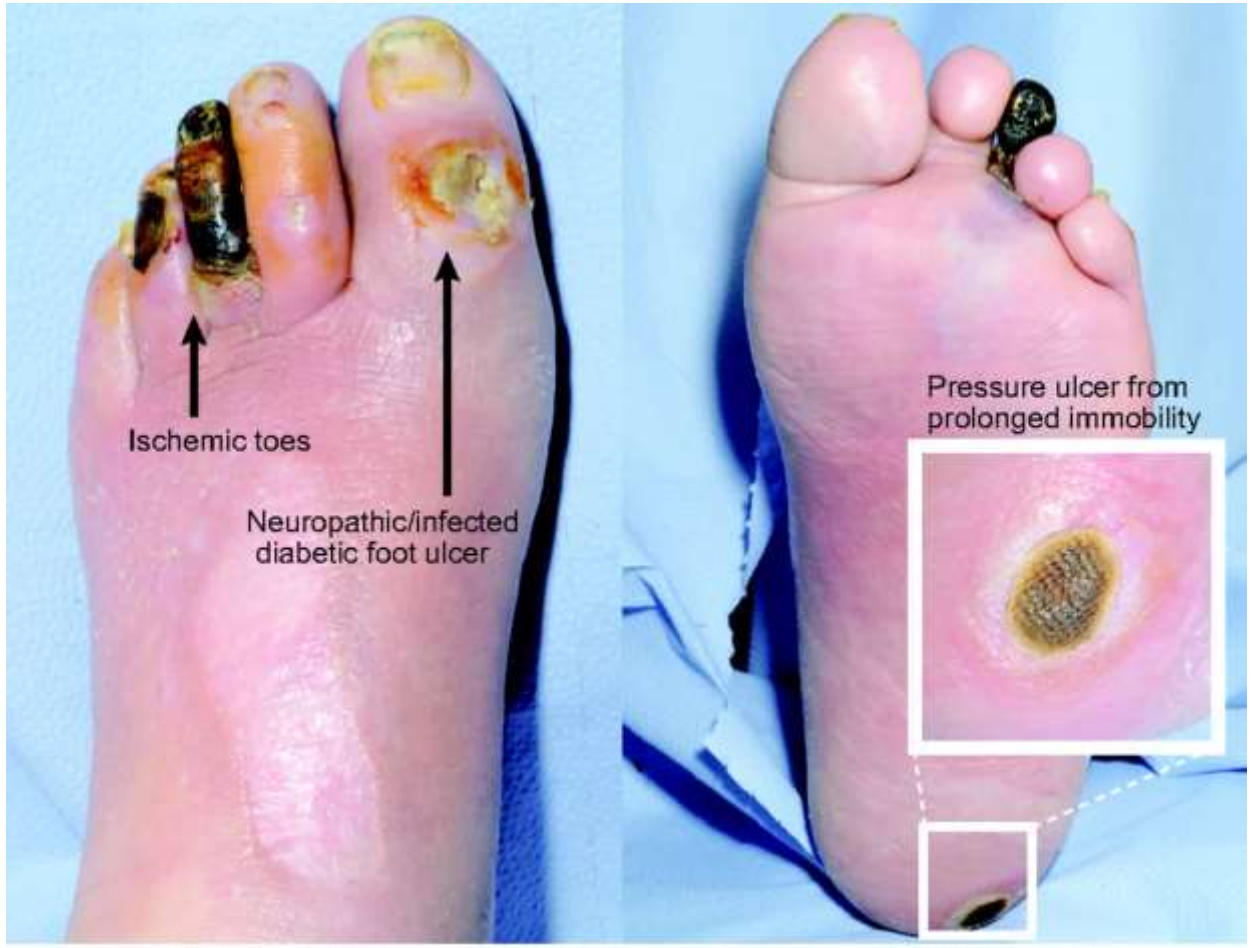
Table 1. CYTOKINE INVOLVEMENT IN WOUND HEALING FUNCTIONS

Healing Function	Cytokines Involved
Inflammatory Cell Migration	PDGF
	TGF-β
	TNF-α
Fibroblast Migration	PDGF
	TGF-β
	EGF
Fibroblast Proliferation	PDGF
	TGF-β
	EGF
	IGF
	TNF-α
	IL-1
Angiogenesis	bFGF (FGF2)
	aFGF (FGF1)
	TGF-β
	TGF-α
	EGF
	TNF-α
	VEGF
	IL-8
	PD-ECGF
Epithelialization	EGF
	TGF-α
	KGF (FGF7)
	bFGF (FGF2)
	IGF
	HB-EGF
Collagen Synthesis	PDGF
	TGF-β
	bFGF (FGF2)
	EGF

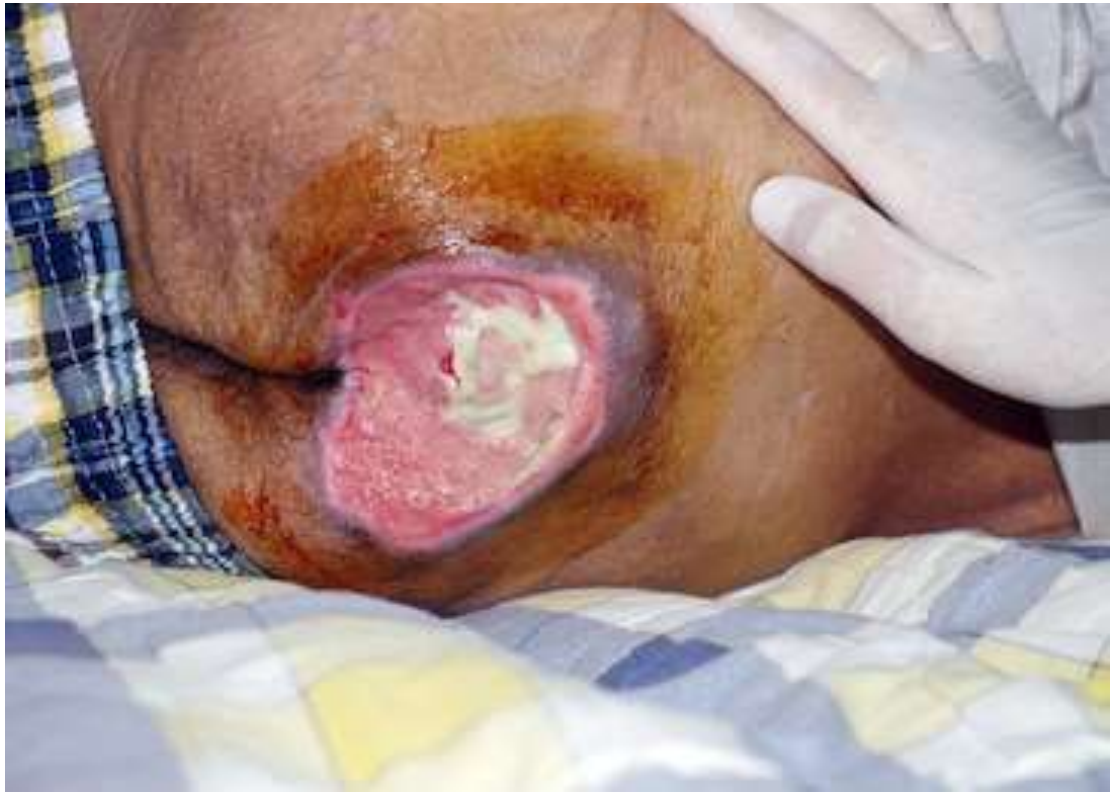
PDGF = platelet-derived growth factor; TGF-β = transforming growth factor-β; TNF-α = tumor necrosis factor-α; EGF = epidermal growth factor; IGF = insulin-like growth factor; IL-1 = interleukin-1; bFGF = basic fibroblast growth factor; aFGF = acidic fibroblast growth factor; TGF-α = transforming growth factor-α; VEGF = vascular endothelial growth factor; IL-8 = interleukin-8; PD-ECGF = platelet-derived-endothelial cell growth factor; KGF = keratinocyte growth factor; and HB-EGF = heparin binding epidermal growth factor.

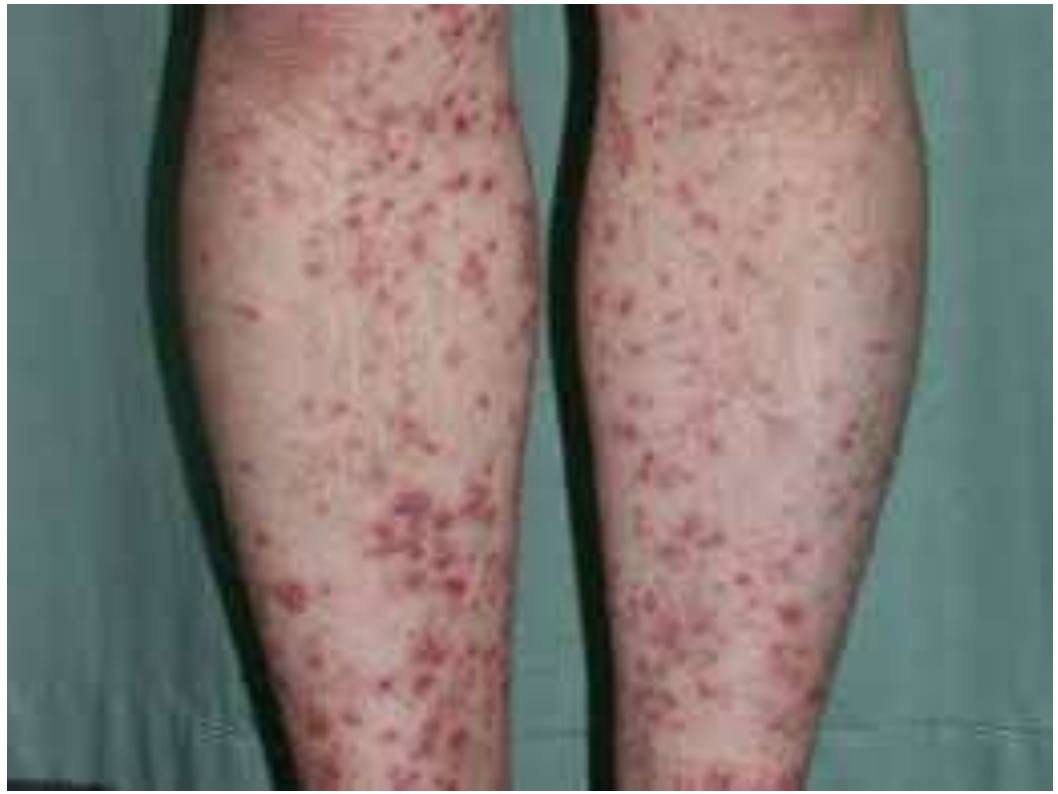
Chronic Wound





Chronic Wound





Factors contributing to impaired wound healing

A. Local factors	B. Systemic factors
❖ Arterial insufficiency ❖ Venus insufficiency ❖ Edema ❖ Infection ❖ Pressure ❖ Radiation ❖ Foreign material ❖ Necrotic tissue	❖ DM ❖ Malnutrition ❖ Vitamin deficiency ❖ Chemotherapy ❖ Smoking ❖ Aging ❖ Steroids

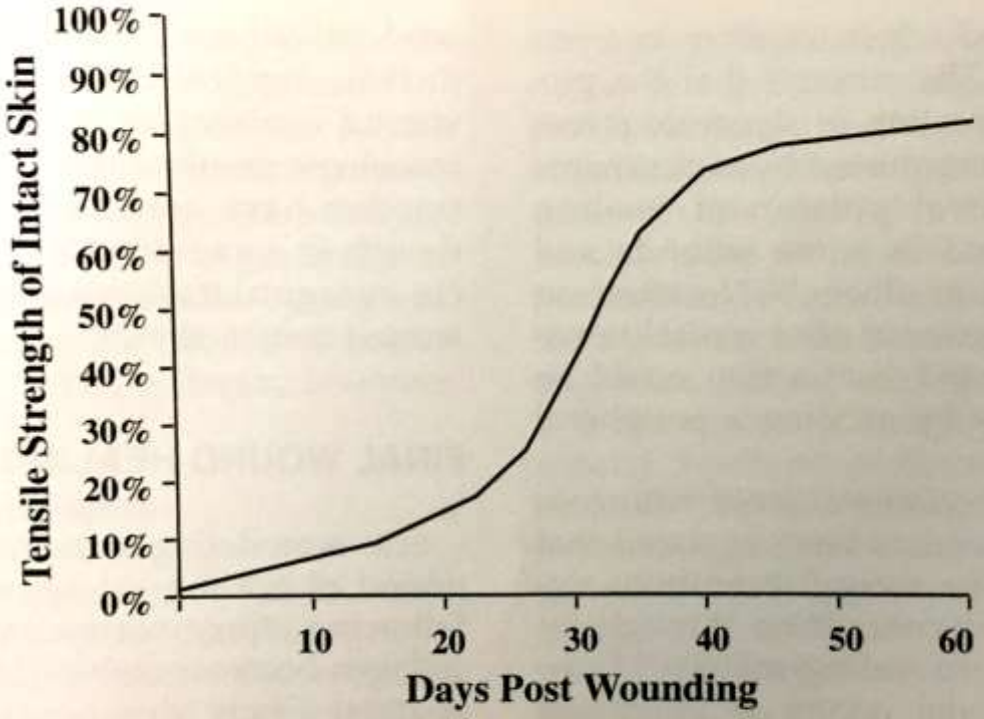


Figure 3. Tensile strength of the healing wound.

Table 1. THE ESTIMATED PREVALENCE AND HEALTH CARE COSTS OF CHRONIC WOUNDS.

Wound Type	Total Prevalence	Estimated Annual Cost
Pressure Ulcer[1]	0.04–0.08%	$1.3 billion
Venous Ulcer[2]	1–2%	$1 billion
Diabetic Ulcer[3]	Total 0.15–0.3% (Diabetics 5–10%)	$1 billion

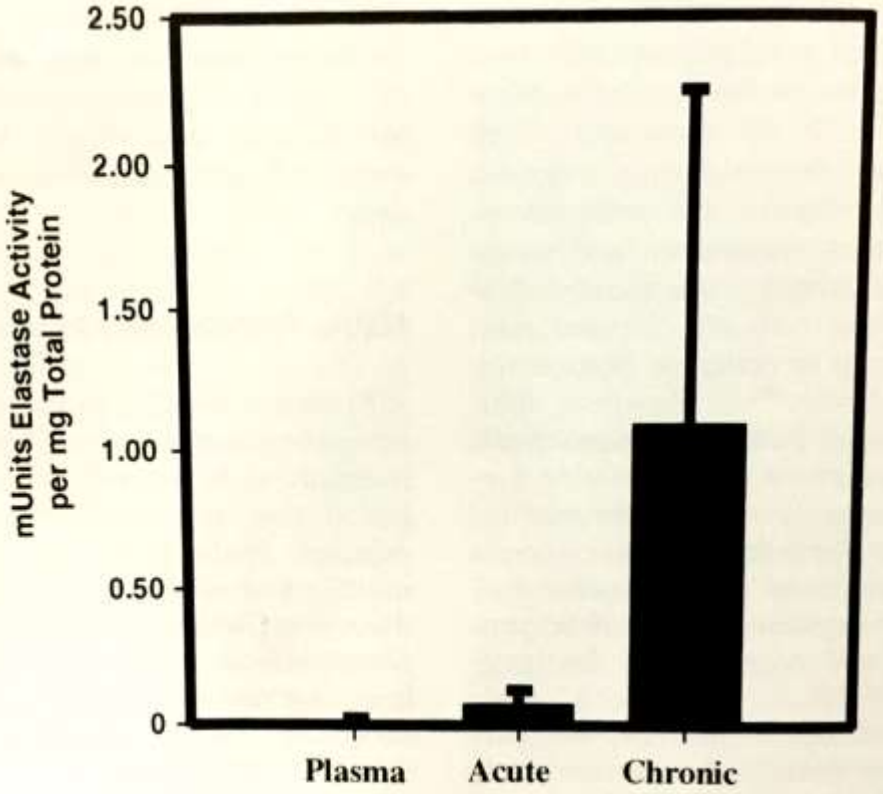


Figure 2. Levels of elastase activity are significantly higher in chronic wound fluid compared with acute wound fluid. Elastase activity was determined by a colorimetric assay using methoxysuccinyl-ala-ala-proval-p-nitoanilide substrate. (*From* Yager DR, Chen SM, Ward BS, et al: Ability of chronic wound fluid to degrade peptide growth factors is associated with increased levels of elastase activity and diminished levels of proteinase inhibitors. Wound Repair and Regeneration 5:23, 1997; with permission.)

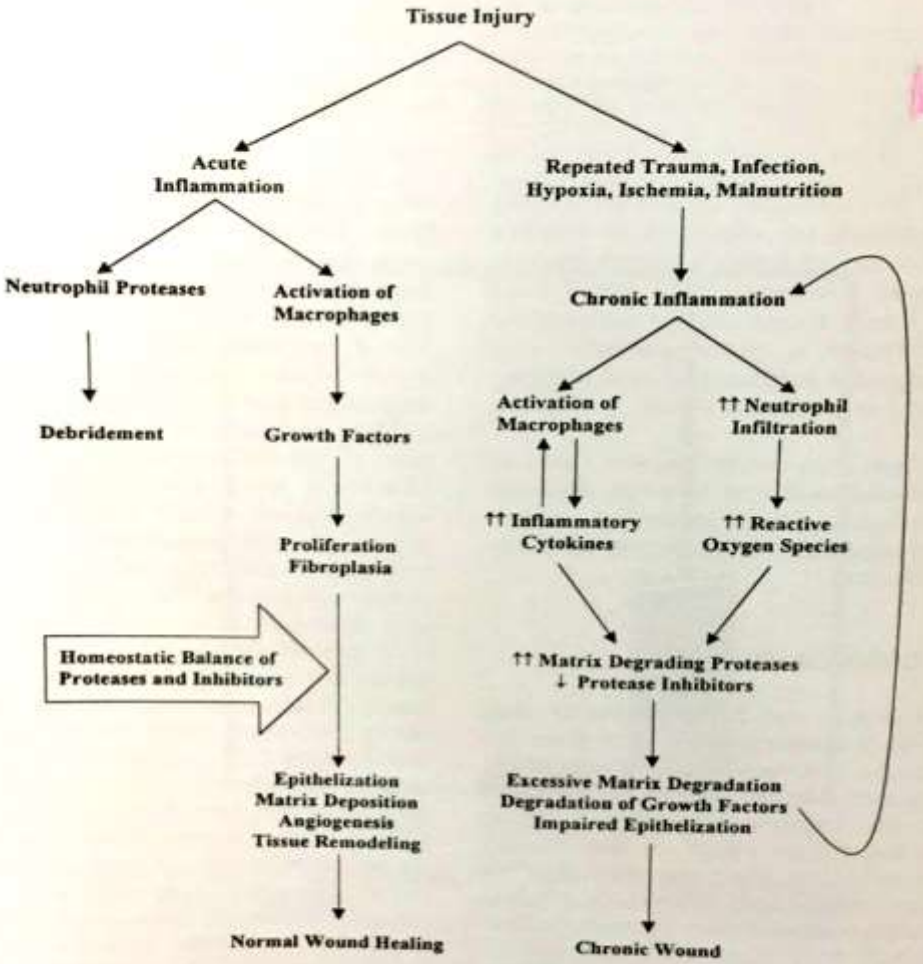


Figure 4. The final common pathway in the pathophysiology of chronic wounds.

Advanced Wound care

1- Hyperbaric Oxygen Therapy

MVHS Advanced Wound Care features cutting edge hyperbaric oxygen therapy (HBOT). This is a treatment in which the patient breathes 100 percent oxygen inside a pressurized chamber.

HBOT quickly delivers high concentrations of oxygen to the bloodstream and assists in the healing process of wounds. It is also effective in fighting certain types of infections, stimulates the growth of new blood vessels and improves circulation.

Conditions for which we provide HBOT at out facility include: compromised skin grafts/flaps, osteomyelitis, diabetic ulcers, late effects of radiation and sensorineural hearing loss.

Throughout HBO therapy, the patients are monitored for any discomfort, hypoglycemia in diabetic patients, and any alarming symptoms.

A typical course of treatment involved the patient spending about 2 hours a day in the chamber, five days a week over a six to eight week period.

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1- **Hyperbaric Oxygen Therapy**

Advanced Wound care

2- **Wound Care Products**

A- Absorbents
B- Impregnated Dressings
C- Transparent Films
D- Foam
E- Hydrogels
F- Xerogels
G- Hydrocolloids

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2- Wound Care Products

Table 4. THE FIVE RULES OF WOUND DRESSINGS

Rule #1: The Rule of Categorization
Learn about dressings by generic category and compare new products with those that already make up the category.

Rule #2: The Rule of Selection
Select the safest, most effective, user-friendly, and cost-effective dressing possible.

Rule #3: The Rule of Change
Change dressings based on patient, wound, and dressing assessment, not on standardized routines.

Rule #4: The Rule of Evolution
As the wound moves through the phases of the wound healing process, evolve the dressing protocol to optimize wound healing.

Rule #5: The Rule of Practice
Practice with dressing materials is required to learn their performance parameters and related tricks-of-the-trade.

From Krasner D: Dressing decisions for the twenty-first century: *In* Krasner D, Kane D (eds): Chronic Wound Care: A Clinical Source Book for Healthcare Professionals (ed 2). Wayne, PA, Health Management Publications, 1997, p 141; with permission.

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2- Wound Care Products

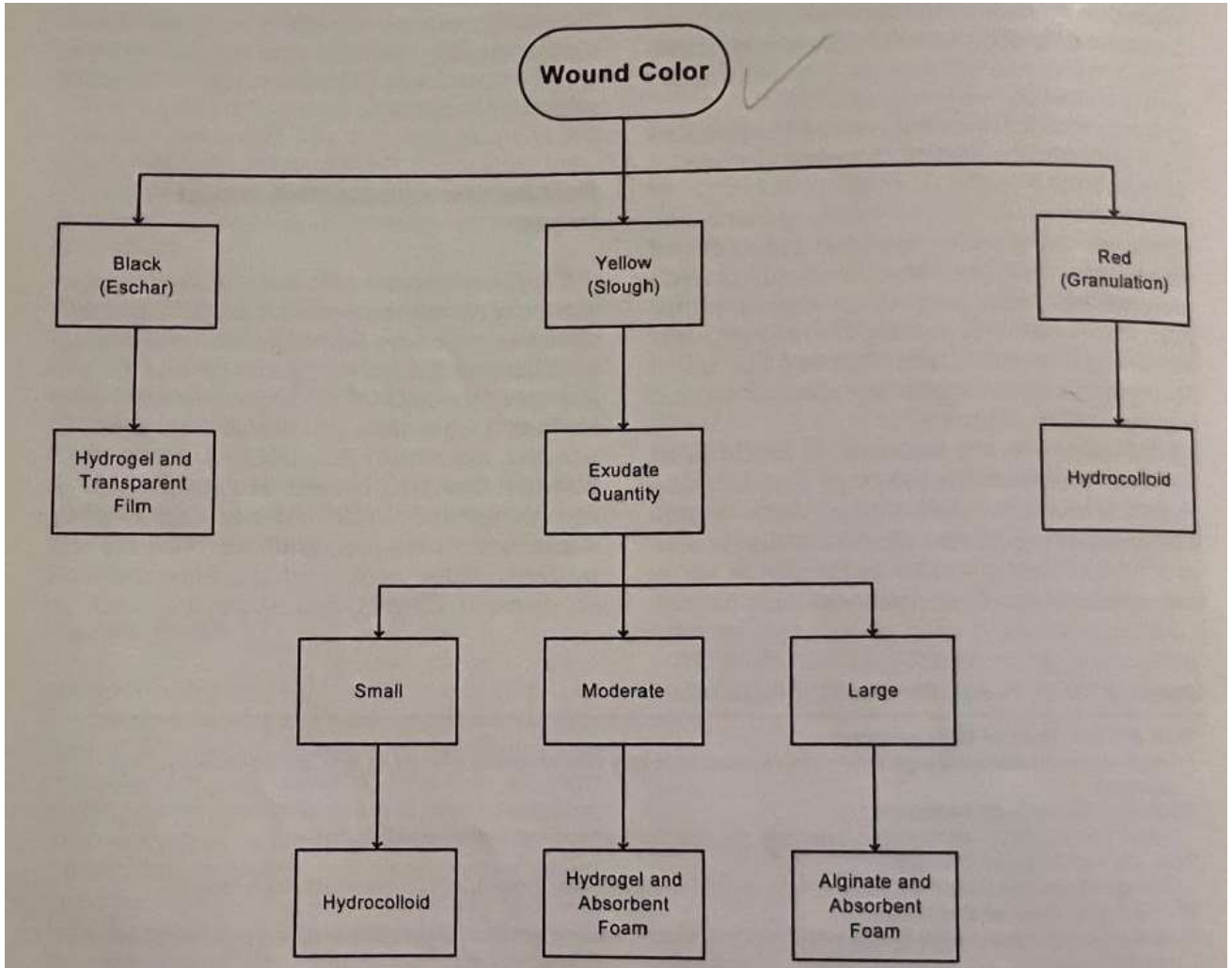

Figure 1. Suggested guidelines for the use of wound products in the full thickness, noninfected, chronic wound (moist wound healing), including dressing types with examples. Hydrogel = Carrasyn; Hydrocolloid = Comfeel; Absorbent Foam = Allevyn; Alginate = Kaltostat; Transparent Foam = Opsite.

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2- Wound Care Products

Table 5. SELECTING THE CORRECT DRESSING AS THE WOUND CHANGES

Wound Condition	Product Selected	Purpose
Hard dry black	Amorphous hydrogel	Hydrate, separate eschar
Exuding yellow	Alginate xerogel	Absorb exudate, autolytic debridement
Moist red	Hydrocolloid	Provide barrier and control humidity
Pink/red	Transparent film	Allow epithelialization, reduce shear

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3- **Exogenous Growth Factors**

A- Platelet-Derived Growth Factor
B- Vascular Endothelial Growth Factor
C- Transforming Growth Factor
D- Epidermal Growth Factor
E- Fibroblast Growth Factor
F- Keratinocyte Growth Factor
G- Insulin-Like Growth Factor

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4- **Skin Replacement**

A- Cultured Epithelium
B- Dermal Replacement
C- Epidermal-Dermal (Composite) Cultured Grafts
E- Integra
F- Alloderm
G- Indoform

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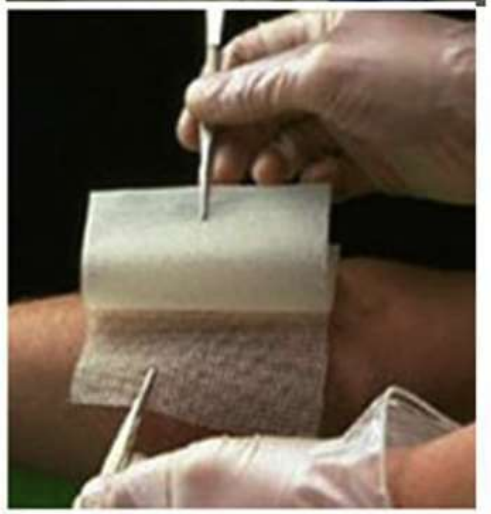
4- **VAC Therapy**



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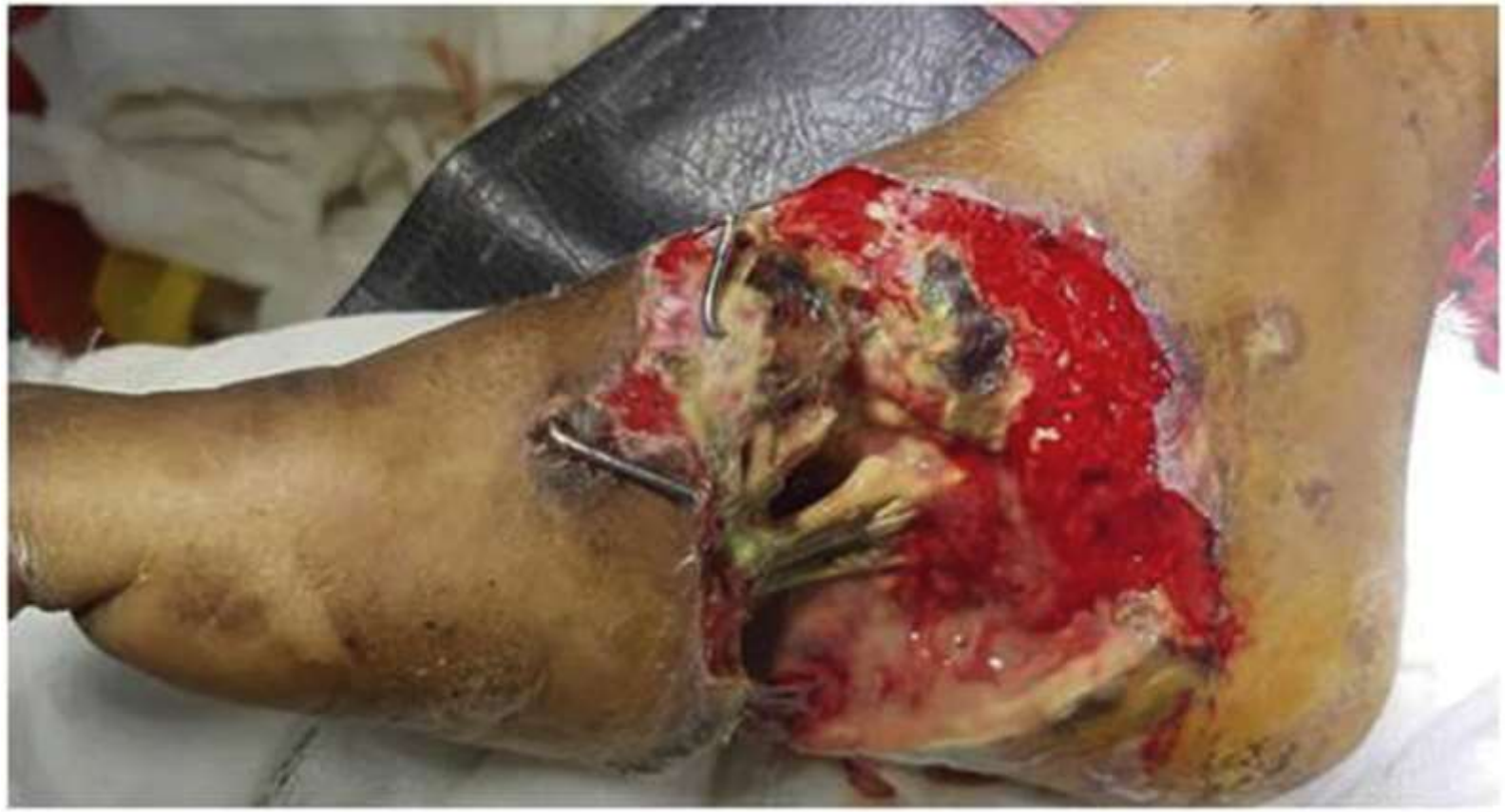
4- **VAC Therapy**



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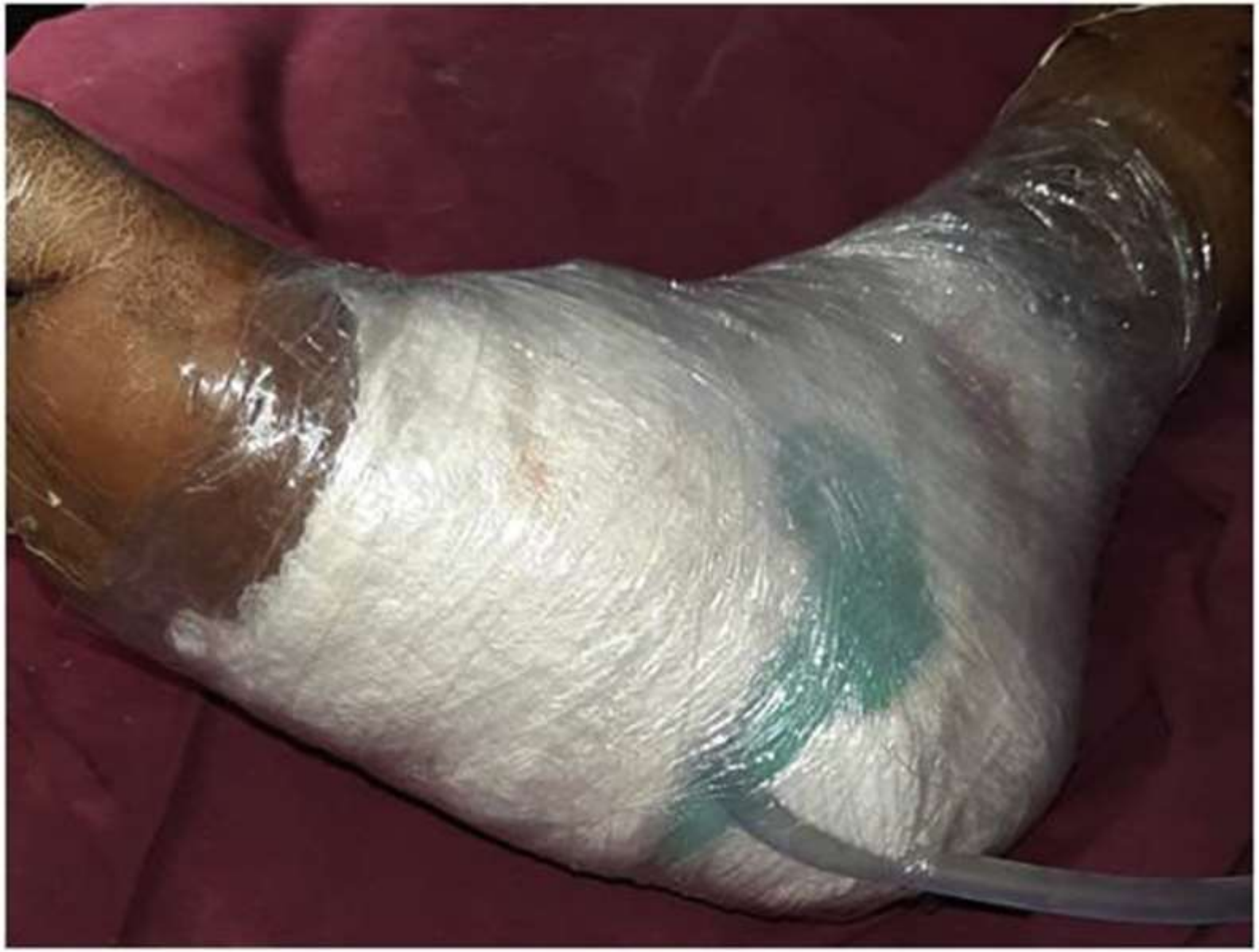
4- **VAC Therapy**



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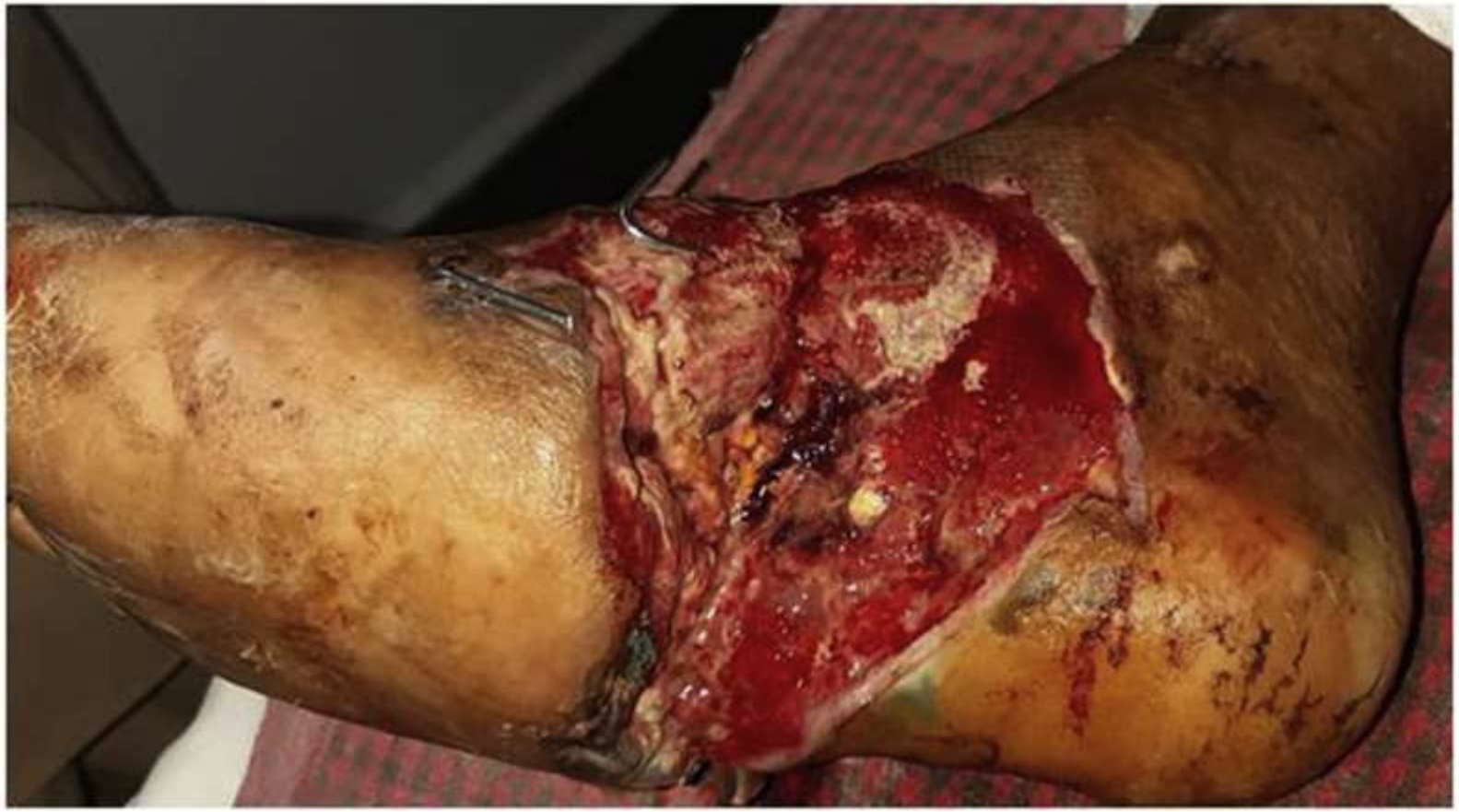
4- **VAC Therapy**



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4- VAC Therapy

Key points

- VAC is a good alternative/adjunct to standard wound care especially for difficult wounds.
- It reduces the extent of reconstructive procedures.
- The optimum pressure setting is 125 mm of Hg.
- Intermittent suction is better than continuous suction.
- There are logistic benefits of VAC over conventional wound care methods.
- Cost of VAC is comparable to standard wound care methods and in long term it has a cost benefits.

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4- VAC Therapy

Conclusions

VAC/NPWT stabilize the wound, reduce edema, reduces the bacterial load, improve tissue perfusion, and stimulate granulation tissue. It will improve the possibility of spontaneous wound healing and reduce the need for major plastic surgical procedures. VAC therapy is simple and effective substitute for the management of various wounds than conventional dressings in terms of reduction in wound size, treatment duration and cost.

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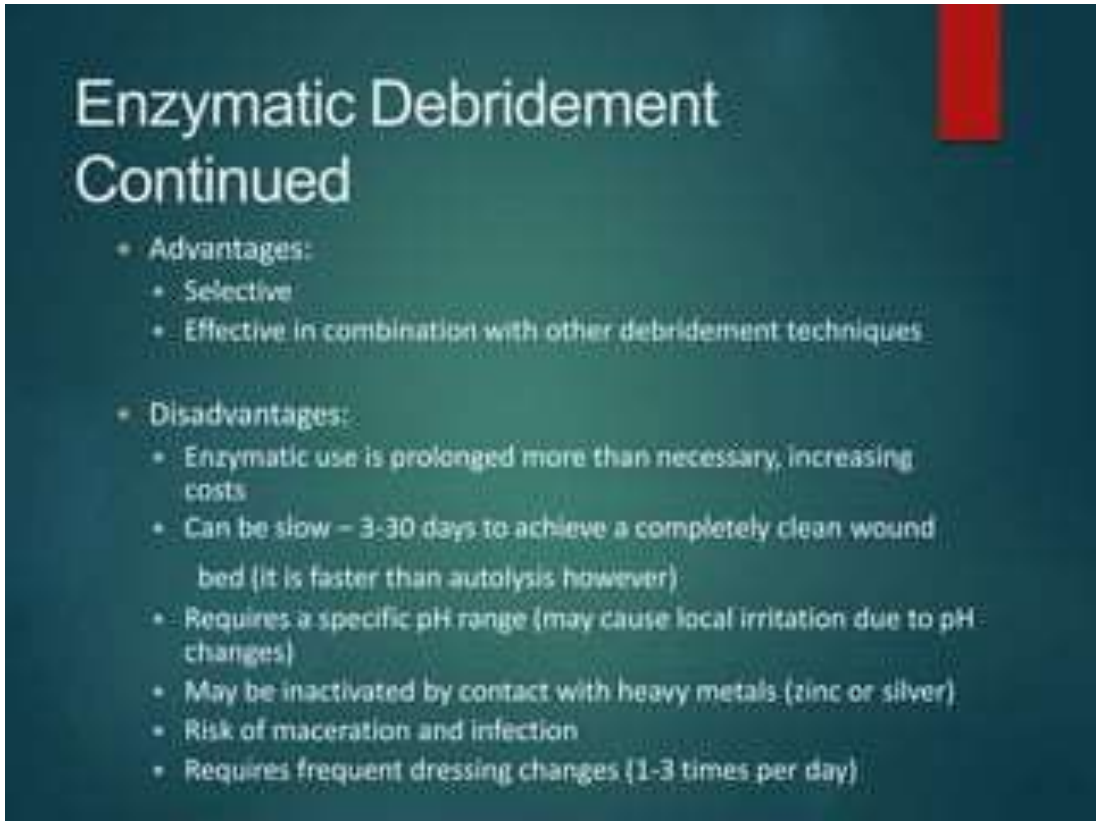
5- **New Debridement Techniques**

- **Enzymatic**
- Autolytic
- Mechanical



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5- **New Debridement Techniques**

- Enzymatic
- **Autolytic**
- Mechanical

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5- **New Debridement Techniques**

- Enzymatic
- Autolytic
- **Mechanical**

Advanced Wound care

6- Biophysical Therapies

- Electrical Stimulation
- Ultrasound Therapy

Electromagnetic Therapy: This process uses the electrical field that develops from exposure to an oscillating magnetic field. The treatment is thought to work by mimicking or enhancing natural wound-induced electrical fields produced in normal human skin.

Ultrasound Therapy :it enhances the degranulation of mast cells resulting in the release of histamine and other mediators that attract fibroblasts and endothelial cells to the injured area. This will later result in the formation of collagen-containing vascular granulation tissue.

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6- AI-Powered Wound Care

AI is transforming wound care:

1. **Wound Assessment & Diagnosis**:
2. **Personalized Treatment**
3. **Remote Monitoring & Telemedicine**
4. **Predictive Analytics**
5. **Reduction in Healthcare Costs**

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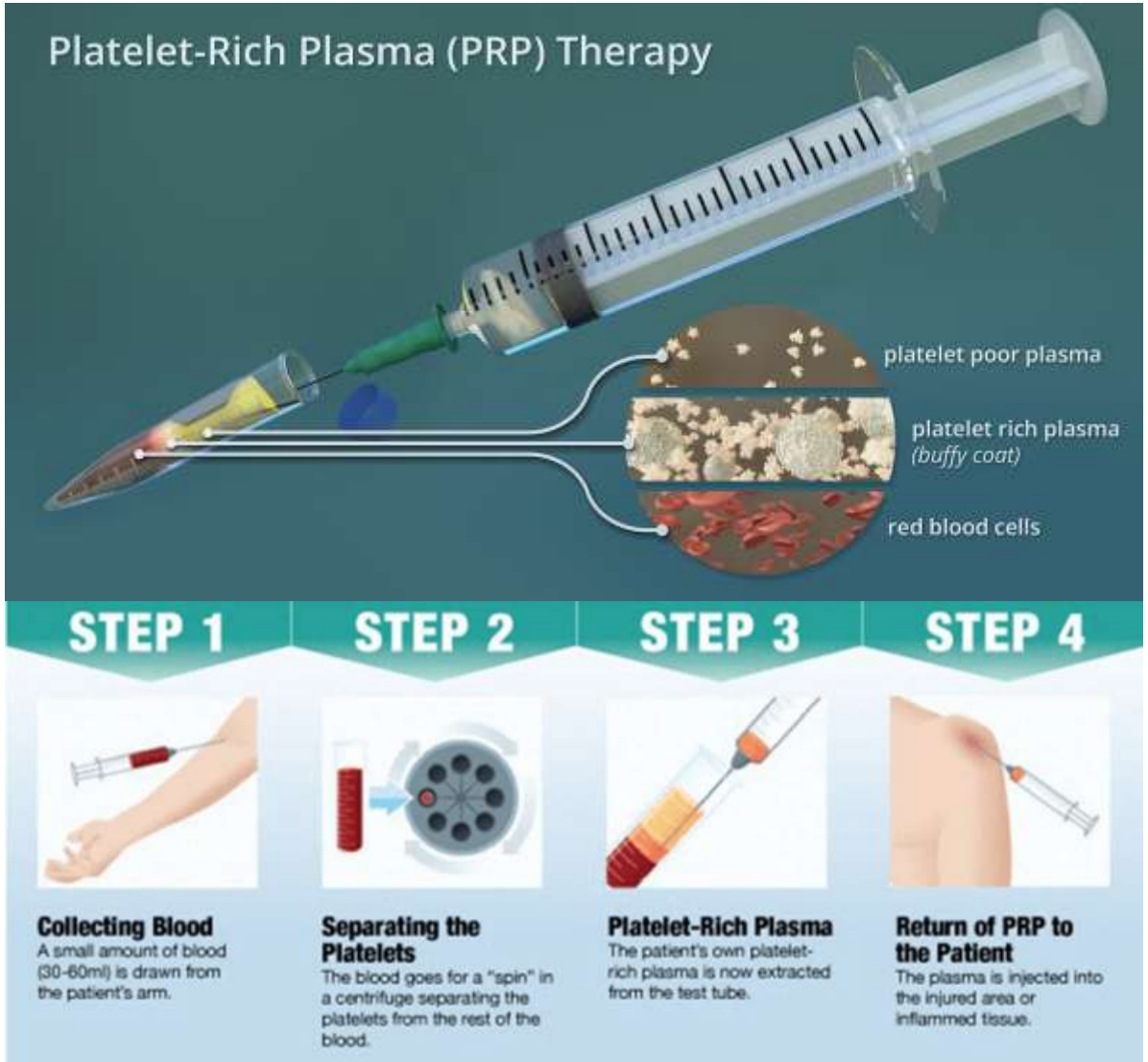
7- **Platelet-rich Plasma (PRP) Therapy**

Platelet-Rich Plasma: Plasma with a high platelet concentration aids wound healing by attracting undifferentiated cells and activating cell division



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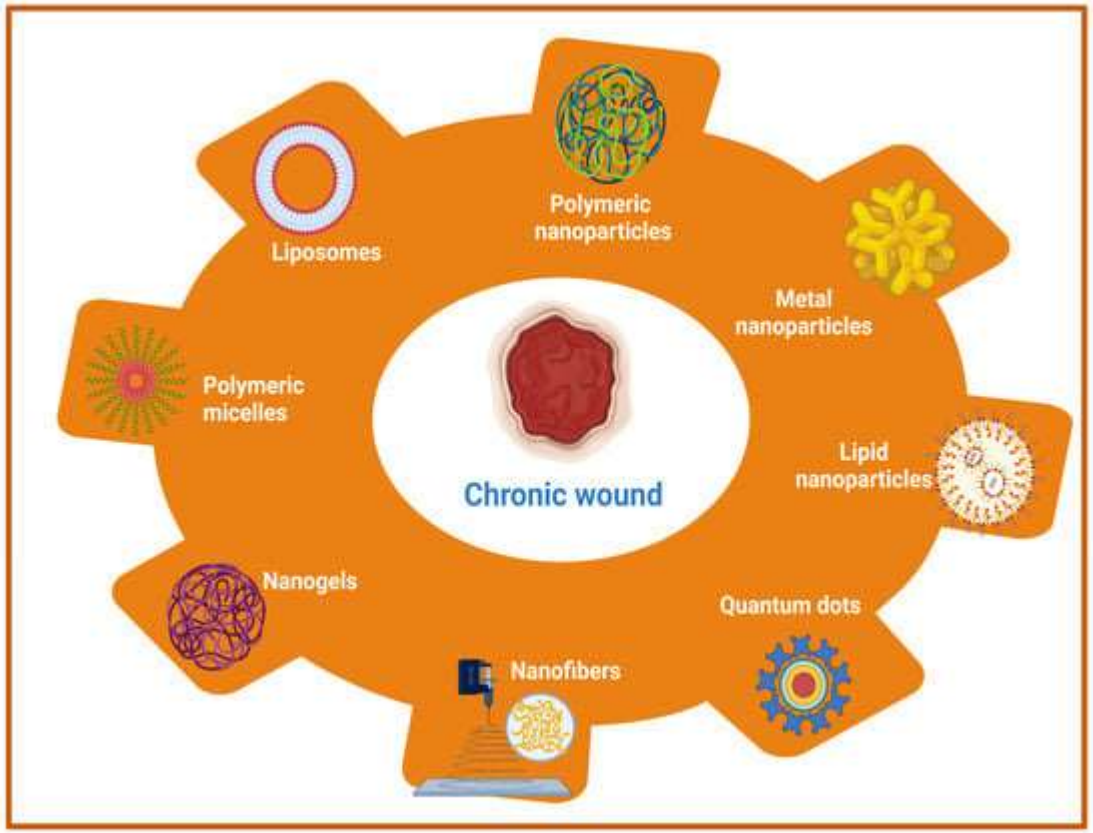
8- **Nanotherapeutics-Based Strategies**

Schematic representation of nanotherapeutic approaches using a wide range of nanomaterials for chronic wound healing.



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9- Stem Cell Therapy-Based Strategies

A representative list of different stem cells-based therapies for accelerated wound healing.

Source of Stem Cells	Type of Wounds	Findings
Bone marrow-derived stem cells	Acute (full thickness wound)	Administration: intradermal and intravenous. Significant improvement in inflammation phase shortening, overexpression of proliferation markers (Ki67, CD71, and CD90), collagen deposition, and granulation tissue re-organization
Bone marrow-derived stem cells and their extracellular vesicles (EVs)	Acute (full thickness wound)	Administration: chitosan/collagen scaffold delivery system. Accelerated wound healing, enhanced collagen deposition
Bone marrow-derived stem cells	Chronic (diabetic wound)	Administration: subcutaneously. Improved collagen deposition and wound healing
Adipose-derived stem cells derived exosomes	Chronic (diabetic wound)	Upregulation and downregulation of specific micro RNAs (miRNAs), Inhibition of inflammation, modulation of PI3K/AKT signaling pathway
Adipose-derived stem cells	Chronic (full thickness burns wound)	Administration: 3D printed scaffold delivery system. Acceleration wound contraction, faster re-epithelialization and healing
Adipose-derived stem cells	Chronic (diabetic wound)	Administration: hydrogel delivery system. Enhanced neo-vascularization and accelerated wound closure
Hair follicles stem cells	Acute (full-thickness excisional wound)	Administration: intradermal injection. Shorter inflammation phase, function vascularization, enhanced re-epithelialization
Hair follicles stem cells	Chronic (venous leg ulcers)	Administration: direct application-hair skin graft. Significant reduction in ulcer area, improved healing
Hair follicles stem cells	Acute (full thickness skin wound)	Administration: direct application-hair skin graft. Overexpression of prostate cancer-upregulated long noncoding RNA 1 (PlncRNA-1), accelerated epidermal regeneration and wound healing
Induced pluripotent stem cells	Acute (full-thickness skin Wounds)	Administration: direct topical application. Expedited wound closure, enhanced collagen deposition
Induced pluripotent stem cell-derived exosomes	Chromic (diabetic ulcers)	Administration: direct. Enhanced migration and proliferation of fibroblasts, accelerated wound healing
Induced pluripotent stem cell-derived microvesicles	Chronic (burn wound)	Administration: Local transplantation. Accelerated wound closure, promotion of keratinocytes migration, increased re-epithelialization,

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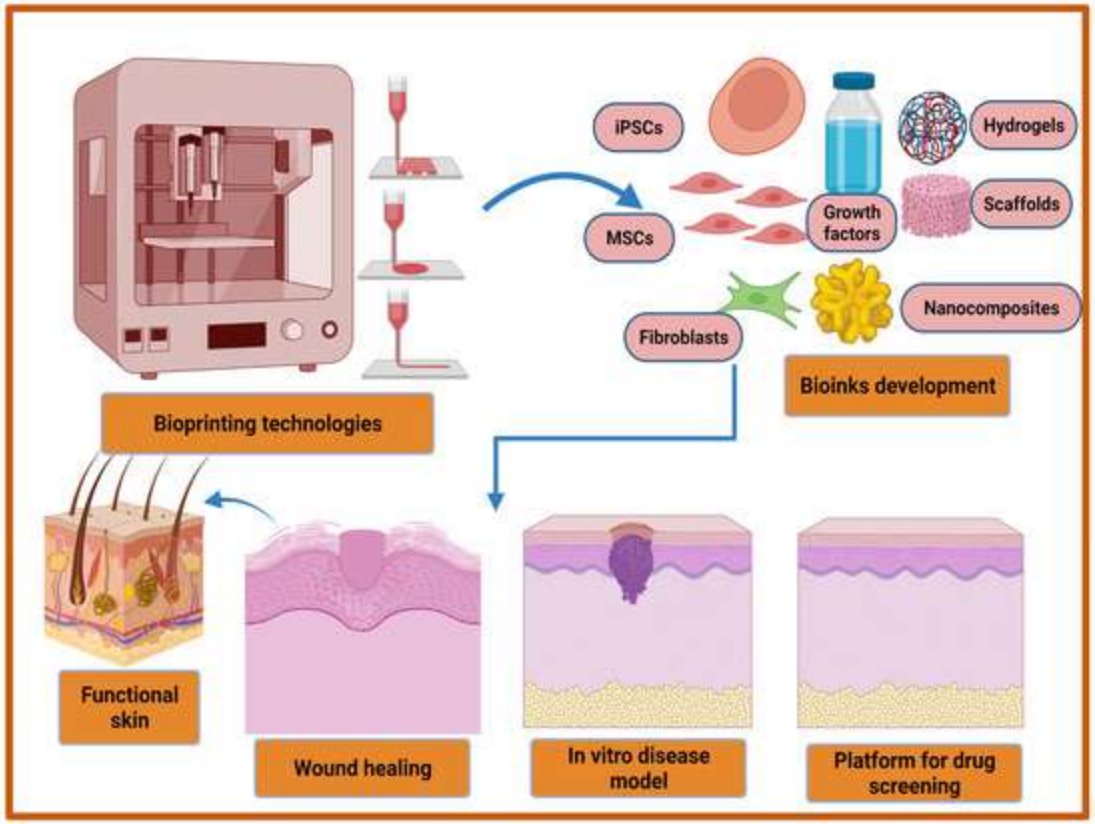
10-Bioprinting-Based Strategies

Recent advancements in 3D bioprinting technologies and bio-inks development for improved wound healing, in vitro disease model development, and the fabrication of high throughput platform for drug screening.



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10-Bioprinting-Based Strategies

A representative list of bio-inks and bioprinting methods for wound healing applications.

Biomaterial/Bioink/Cells	Bioprinting Method	Type of Wound	Findings
Fibrin and collagen hydrogel (Fibroblasts and keratinocytes)	In situ extrusion bioprinting	Acute (full thickness skin wound)	Rapid wound closure, reduced contraction, and accelerated re-epithelialization
Fibrin hydrogel with gelatin, glycerol, and hyaluronic acid (Keratinocytes, melanocytes, fibroblasts, follicle dermal papilla cells, and microvascular endothelial cells, preadipocytes.)	Extrusion bioprinting	Acute (full thickness skin wound)	Accelerated wound closure, promotion of epidermal barrier formation, reduction in wounds contraction, remodeling of collagen
Gelatin/sodium alginate/gelatin methacrylate hydrogel (Dermal fibroblasts and epidermal keratinocytes)	Extrusion bioprinting	Acute (full thickness skin wound)	Reduced wound contraction and scarring, enhanced skin epithelialization, accelerated wound healing
Plasma-derived fibrinogen-containing factor XIII, fibronectin, thrombin, and macrophages (FPM bioink) (Primary fibroblasts human endothelial cells, and keratinocytes)	Extrusion bioprinting	Acute (full thickness skin wound)	Rapid wound closure and facilitation of re-epithelialization process
Fibrinogen/collagen hydrogel (Fibroblasts and keratinocytes)	In situ inkjet bioprinting	Acute (full thickness skin wound)	Improved wound closure and re-epithelialization process
Fibrin-collagen hydrogel (Amniotic fluid-derived stem (AFS) cells and bone marrow-derived mesenchymal stem cells (MSCs)	In situ extrusion bioprinting	Acute (full thickness skin wound)	Enhanced angiogenesis and wound closure rates
Skin-derived extracellular matrix (S-dECM) bio-ink (Fibroblasts, keratinocytes, endothelial progenitor cells and adipose-derived stem cells (ASCs)	Extrusion and inkjet bioprinting	Acute (full thickness skin wound)	Accelerated wound closure, enhanced re-epithelization, and neovascularization
Living photosynthetic microalgae scaffolds	In situ bioprinting	Chronic (diabetic wound)	Significantly reduced local hypoxia, accelerated chronic wound closure increased angiogenesis, and enhanced extracellular matrix (ECM) synthesis
Sodium alginate/gelatin/collagen hydrogel (Fibroblasts and keratinocytes)	Extrusion bioprinting	Acute (full thickness skin wound)	Enhanced re-epithelialization, reduced skin wound contraction, and accelerated wound healing
Strontium silicate (SS) microcylinders (Fibroblasts and keratinocytes)	Extrusion bioprinting	Acute and chronic wounds	Outstanding angiogenesis and wound healing