

# Study on Healing Treatment of Chronic Wound

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**Abstract:** Chronic wound is one of the difficulties in clinical treatment. The complex pathological mechanism of chronic wound involves many links, such as inflammation disorder, cell proliferation obstruction, insufficient angiogenesis and abnormal matrix remodeling. In recent years, with the rapid development of molecular biology, regenerative medicine and materials science, researchers have made remarkable breakthroughs in the molecular regulation of wound healing, the application of growth factors and new biological dressings. These advances not only deepen the understanding of the mechanism of chronic wound formation and extension, but also provide theoretical basis and technical support for the study of more effective and safe treatment strategies. In the future, further optimization of treatment strategies to promote rapid and functional wound healing will be the focus of research in this field. The purpose of this paper is to summarize the current research on chronic wound healing treatment, provide clinicians with theoretical and practical guidance on chronic wound treatment, and provide valuable reference for future research direction exploration and expansion.

**Keywords:** Chronic Wound; Wound Healing; Formation Mechanism; Heal.

## 1. Introduction

Chronic wound, also known as chronic ulcer or chronic refractory wound, refers to the pathological state of the wound in the normal healing process, due to a variety of factors that lead to the repair process is blocked, thus delaying healing or unable to heal. Such wounds not only bring long-term physical pain to the patients, but also seriously affect their mental health, and cause a heavy economic burden to the family and society. With the aggravation of population aging and the increase of chronic diseases, the incidence of chronic wounds has increased year by year, and has become another "killer" endangering human health after cancer, cardiovascular disease, obesity and diabetes. Therefore, in-depth research on the mechanism of chronic wound healing and its treatment strategies is of great significance for improving patients' quality of life and reducing social burden [1]. In this context, this article reviews the treatment of chronic wound healing, aiming to provide the basis for the clinical treatment of this patient.

## 2. Physiological Process of Chronic Wound Formation

Wound healing is a complex and delicate biological process, covering four stages: hemostasis, inflammation, hyperplasia and maturity, all of which synergistically promote wound healing and tissue regeneration [2-5]. The hemostasis period begins within a few hours after injury, and the key task is to seal the wound, which is also a crucial link [6]. Blood clots are formed through platelet aggregation and activation of the clotting system to stabilize the wound and lay the foundation for the subsequent stage [7]. The inflammatory period follows the hemostatic period and lasts for 4-6 days. It mainly removes bacteria, necrotic tissues and foreign bodies, and prepares the environment for subsequent repair through inflammatory response [8]. The proliferative phase begins about 48 hours after trauma and lasts for 2-3 weeks. It is

characterized by the growth of blood vessels and granulation tissues, which provide nutrients to the wound, promote healing and prevent infection [9,10]. The maturity stage, also known as the epithelial formation stage, is the final stage of the physiological process, indicating that the wound is close to complete repair [11], involving the maturation of granulation tissue, epithelial cell coverage and scar formation, and may last for a long time, especially for chronic and refractory wounds [12,13].

## 3. Pathophysiological Mechanism of Chronic Wound Formation

The mechanism of chronic wound formation is complex, involving local tissue hypoxia, sustained action of inflammatory factors, growth factor deficiency and bacterial biofilm formation [14]. After injury, wound repair requires a large amount of oxygen, resulting in the formation of a local hypoxic environment on the wound, which will inhibit angiogenesis and cell proliferation and hinder healing [15-17]. There may be bacterial biofilm on the surface of the wound, which is difficult to be cleared by antibiotics due to its special structure, thus causing sustained inflammatory response [18,19]. The failure of inflammatory factors to subside prevents the transformation of M1-type macrophages into M2-type macrophages, keeps the wound in a stage of continuous inflammation, which is difficult to heal, destroys the normal repair process of the wound, and leads to the obstruction of cell proliferation and matrix deposition [20]. As an important signaling molecule in vivo, growth factor (GF) can effectively activate and stimulate target cells, promote their division and proliferation, repair various damaged tissues, enhance extracellular matrix synthesis and secretion, and provide a solid material basis for the repair of damaged tissues. The lack of growth factors directly affects cell proliferation and matrix deposition, thus affecting the speed and quality of wound healing [21,22]. The formation of biofilm not only increases bacterial resistance to antibiotics,

but also enables bacteria to evade clearance by the host immune system, aggravate inflammation, release toxins, and further deteriorate the wound environment, which jointly leads to the obstruction of wound healing and the formation of chronic wounds [23,24].

#### **4. Traditional Treatment of Chronic Wound Healing**

Debridement is the most basic way of chronic wound healing treatment, which involves thorough cleaning, decontamination and excision of dead tissues [25]. In clinical practice, the most commonly used methods include surgical debridement, mechanical debridement, enzymatic debridement, autolytic debridement and biological debridement [26]. Surgical debridement, which involves repeated irrigation, removal of necrotic tissue, and suturing or drainage, is suitable for heavily contaminated or deep wounds [25]. Mechanical debridement is the use of physical methods, such as gauze friction, high pressure pulse and ultrasonic spray, to remove dead tissue and foreign bodies on the surface of the wound. It is often used to assist surgical debridement when the wound surface is lightly polluted and there is not much necrotic tissue [27,28]. Enzymatic debridement uses exogenous enzymes to degrade necrotic tissue, which is suitable for patients who are intolerant to surgery, especially elderly or long-term care patients, but not for deep exposure or rapid debridement [29]. Autolytic debridement is the use of wet dressings to gently separate necrotic tissue in a moist wound environment, hydrate dry and deactivated tissue, promote necrotic tissue to detach from normal tissue, and gradually be engulfed and cleared by cells around the wound. It is often used in some patients who are not suitable for surgical debridement, such as patients with bleeding tendency; Although autolytic debridement has a slower onset, it is still valuable for some patients [30]. Biological debridement is the removal of dead tissue using maggots bred in a sterile environment, such as the larvae of *Lucilia sericata*. Maggots act as debridements by devouring and digesting dead tissue and pathogenic microorganisms. It is often used for necrotic, infected or chronic non-healing wounds. However, it requires strict aseptic operation and professional nursing knowledge to ensure patient safety and efficacy [31]. Hyperbaric oxygen therapy uses high pressure environment to inhale pure oxygen to achieve therapeutic effect [44]. It accelerates wound healing by correcting hypoxia, resisting infection, promoting blood vessel and granulation growth and other mechanisms [32,33]. It has been widely used in the treatment of chronic trauma such as pressure ulcers and diabetic feet with remarkable results [34]. Negative pressure wound therapy (NPWT Negative Pressure Wound Therapy) is a kind of using special foam dressings, use transparent sticker to close the wound, and through the negative pressure pump in wound area form a continuous or intermittent negative pressure, so as to promote the wound healing therapy, 1994, It was first introduced to our country by Professor Jude [35]. It can effectively drain exudate and bacteria, keep the wound clean and dry, and reduce infection [36]. The negative pressure environment accelerates blood circulation, provides more nutrients to the wound, reduces edema, and promotes cell repair. This technology reduces fluid seepage and odor, reduces the frequency of dressing changes, and relieves patients' pain [37]. Kangfu new solution is derived from the extract of *Periplaneta Americana* and is rich in polyols,

growth factors and various amino acids, which effectively promote the growth of granulation tissue and accelerate wound healing [38]. It can clear dead tissue, suppress inflammation, reduce edema, enhance anti-infection ability, and regulate immune function. Especially for chronic wounds, healing new solution can improve microcirculation, increase blood supply, provide adequate nutrition and oxygen for tissue repair, and accelerate the recovery process [39,40].

#### **5. Future Prospects of Chronic Wound Healing Treatment**

##### **5.1. Growth Factors**

Vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), epidermal growth factor (EGF), transforming growth factor  $\beta$  (TGF- $\beta$ ), granulocyte macrophage colony-stimulating factor (GM-CSF), connective tissue growth factor (CTGF) and other growth factors are overseen in wound healing. They play an important role in the process [21]. Growth factor has been widely used in the treatment of chronic wounds, and its clinical effect and safety have been widely recognized. By promoting cell proliferation and differentiation, growth factors promote collagen synthesis, accelerate wound re-epithelialization, promote granulation tissue formation and angiogenesis, thus shortening wound healing time. In the treatment of chronic refractory wounds such as diabetic foot ulcers and venous ulcers, growth factor has shown remarkable efficacy. It can also participate in the process of tissue remodeling by regulating the balance of synthesis and degradation of extracellular matrix, which helps to reduce the formation of scar tissue and improve the appearance of scar. Compared with traditional debridement treatment, growth factor treatment has the advantages of rapid action, significant effect and few side effects [41]. Growth factor can be combined with other treatment methods (such as negative pressure wound treatment, surgical treatment, etc.) to further improve the therapeutic effect.

##### **5.2. New Biological Dressing**

New biological dressings refer to wound covering materials with special functions and excellent properties developed by using modern biotechnology and material science [42]. These dressings have demonstrated significant advantages in promoting wound healing, preventing infection, and reducing patient suffering. For example, hydrogel dressings have become the focus of research in recent years because of their good moisture retention, biocompatibility and drug release control ability. With the advancement of materials science, the properties of hydrogel dressings are continuously optimized, such as enhanced water absorption, air permeability and antibacterial properties. It is widely used in the treatment of burns, wounds, diabetic feet and other wounds that are difficult to heal. They can keep the wound moist, promote cell proliferation and migration, and accelerate wound healing [43]. Silver ion dressing uses the broad-spectrum antibacterial properties of silver ions to effectively inhibit bacterial growth and reduce the risk of wound infection. With advances in technology, new silver ion release techniques have made dressings more efficient and safer. According to Huang Yuanmei et al. [44], silver ion dressings have been widely used in burn treatment, chronic wound care and other fields. Not only do they have antibacterial effects, they also promote wound healing and

reduce scar formation. Drug-loaded dressings are special medical dressings, which directly apply or impregnate drug ingredients on the dressings, thus giving the dressings more additional effects, such as chitosan dressings with good biocompatibility and biodegradability. Antibiotics such as levofloxacin, ciprofloxacin, minocycline and gentamicin can be mixed into chitosan to prepare traditional Chinese medicine oil dressings with antibacterial, hemostatic and anti-inflammatory properties and promote wound healing. Traditional Chinese medicine oil dressings, such as purple yusan butter gauze, etc., are directly applied on the dressings, and wounds can be treated by utilizing the anti-inflammatory, analgesic and healing properties of traditional Chinese medicine. There are erythromycin dressings, etc., which directly apply the drug ointment with antibacterial and anti-inflammatory effects to the wound to achieve the purpose of treatment. These dressings have the advantages of high local drug concentration, reducing adverse reactions, and promoting wound healing [5].

### 5.3. Regenerative Medicine Technology

Regenerative medicine promotes the regeneration and repair of damaged tissues by activating endogenous stem cells or implanting exogenous stem cells or tissue engineering products. This is of great significance for chronic, refractory wounds [45]. Traditional wound repair methods often leave obvious scars, affecting the appearance and function. According to the research of Academician Fu Xiaobing et al. [46], regenerative medicine technology can induce tissue regeneration, reduce scar formation, and improve the quality of wound repair. Combined with stem cells, growth factors and other bioactive factors, regenerative medicine technology can significantly improve the speed of wound healing and treatment efficiency. But. Regenerative medicine technology involves the cross-integration of multiple disciplines, which is difficult in technology and has a long R&D cycle [47]. At present, the high production cost of regenerative medicine products leads to expensive market prices, which limits their wide clinical application.

### 5.4. Interdisciplinary Cooperation

The importance of interdisciplinary cooperation in the treatment of chronic wounds has become increasingly prominent. Chronic wound treatment involves many disciplines, including surgery, dermatology, endocrinology, vascular surgery, rehabilitation and so on. Interdisciplinary cooperation can integrate the resources and advantages of various disciplines, form a joint force, and provide patients with more comprehensive and accurate treatment programs [48]. Through the joint participation and discussion of multidisciplinary experts, a more scientific and reasonable treatment plan can be formulated to reduce misdiagnosis and missed diagnosis and improve the therapeutic effect. For example, in the treatment of diabetic foot, endocrinologists are responsible for controlling blood sugar, vascular surgeons are responsible for improving lower limb blood circulation, surgeons are responsible for wound debridement and repair, and rehabilitation doctors are responsible for patient rehabilitation training. This multidisciplinary cooperation model can significantly improve the healing rate of diabetic foot. At the same time, interdisciplinary cooperation not only helps to improve the therapeutic effect, but also promotes the exchange and cooperation among various disciplines and promotes the development and progress of related disciplines

[26,49]. Through joint research and discussion, new treatment methods and techniques can be found, and new vitality can be injected into the development of chronic wound treatment.

### 5.5. Comprehensive Treatment Strategy

The treatment of chronic wounds should first identify the etiology and treat the etiology. For example, for diabetic foot patients, it is necessary to control blood sugar and improve blood circulation in lower limbs; For patients with pressure ulcer, it is necessary to relieve pressure factors [50]. At the same time, symptomatic treatment should be performed according to the specific conditions of the wound, such as debridement, dressing change, and the use of growth factors [51]. This combination of etiological treatment and symptomatic treatment can significantly improve the healing rate of chronic wounds. In the treatment of chronic wounds, it is often necessary to use multiple treatment methods. For example, in addition to drug therapy, physical therapy (such as negative pressure wound treatment technology), surgical treatment (such as skin grafting, flap repair, etc.), nutritional support and other means can be used. These methods work together and complement each other, which can form a more comprehensive and effective treatment plan and promote wound healing. Develop a personalized treatment plan: The specific circumstances of each patient are different, so it is necessary to develop a personalized treatment plan according to the specific circumstances of the patient. This includes the formulation of treatment plan, the choice of treatment means, the grasp of treatment opportunity and so on. Through the formulation and implementation of personalized treatment plans, the needs of patients can be better met, and the therapeutic effect and patient satisfaction can be improved [28,52,53].

## 6. Summary

With the rapid economic development, the aging of the population and the increase of chronic diseases, more and more patients with chronic refractory wounds caused by diabetes, trauma, pressure, infection, vascular disease and other factors, and their formation mechanism is complex, which is related to tissue hypoxia, the lack of inflammatory factors, growth factors, bacterial biofilm formation and so on. The disease causes long-term physical suffering, seriously affects the mental health of sufferers and imposes a heavy economic burden on families and society. In recent years, debridement is the basic surgical treatment in clinical practice, which can also be combined with auxiliary treatment such as hyperbaric oxygen, growth factor, NPWT and rehabilitation liquid. No matter what kind of treatment method is used, keeping the wound clean and dry is the most critical, and various treatment methods have achieved certain results in treatment. However, it is still necessary to formulate an adapted treatment plan according to the specific situation of the patient. At present, clinical research should further explore the directions of individualized treatment strategies, research and development of new biomaterials, regenerative medicine technology, and interdisciplinary cooperation and integration, so as to improve the speed and quality of chronic wound healing, provide patients with better treatment effects, shorten hospital stay, reduce burden, and improve patient satisfaction.

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