Materials Science and Engineering C 48 (2015) 651–662

Contents lists available at ScienceDirect

Materials Science and Engineering C

journal homepage: www.elsevier.com/locate/msec

Review

Current wound healing procedures and potential care

Michael B. Dreifke [a], Amil A. Jayasuriya [b], Ambalangodage C. Jayasuriya [a,*]

[a] Department of Orthopaedic Surgery, College of Medicine and Life Sciences, The University of Toledo, Toledo, OH 43614-5807, USA
[b] Undergraduate Program, Department of Human Evolutionary Biology, Harvard University, Cambridge, MA 02138, USA

ARTICLE INFO

Article history:
Received 19 August 2014
Received in revised form 5 December 2014
Accepted 17 December 2014
Available online 19 December 2014

Keywords:
Growth factors
Wound healing
Chronic wounds
Wound dressings
Stem cells
siRNA
Sensors

ABSTRACT

In this review, we describe current and future potential wound healing treatments for acute and chronic wounds. The current wound healing approaches are based on autografts, allografts, and cultured epithelial autografts, and wound dressings based on biocompatible and biodegradable polymers. The Food and Drug Administration approved wound healing dressings based on several polymers including collagen, silicon, chitosan, and hyaluronic acid. The new potential therapeutic intervention for wound healing includes sustained delivery of growth factors, and siRNA delivery, targeting microRNA, and stem cell therapy. In addition, environment sensors can also potentially utilize to monitor and manage microenvironment at wound site. Sensors use optical, odor, pH, and hydration sensors to detect such characteristics as uric acid level, pH, protease level, and infection — all in the hopes of early detection of complications.

Contents

1. Introduction

The skin serves its primary function as a protective barrier against environmental insult. When the structural integrity of the skin is compromised its primary responsibility to the immune system is impacted

* Corresponding author at: The University of Toledo, Department of Orthopaedic Surgery, 3000 Arlington Avenue, Toledo, OH 43614-5807, USA.
E-mail address: a.jayasuriya@utoledo.edu (A.C. Jayasuriya).

http://dx.doi.org/10.1016/j.msec.2014.12.068
0928-4931/

leading to serious morbidity and mortality [1–3]. With one-third of the adult population currently living with diabetes and 6.5 million cases of chronic skin ulcers yearly, investigations into the processes involved in wound healing have taken on a more prominent role in recent years [1].

Chronic wounds are frequently being described as an epidemic as they are diagnosed at an alarming rate and causing an enormous burden to the financial structure of our healthcare economy. Due to an aging population and an increased incidence of both diabetes and obesity worldwide, the financial burden of treating chronic wounds has risen dramatically. It is estimated that over $25 billion is spent each year on the treatment of chronic wounds alone. The costs are even more staggering when one factors in loss of productivity for affected individuals as well as long-term facility and nursing home care [4]. Estimates of the lifetime probability of diabetics developing a chronic foot ulcer are between 10 and 25% [5,6]. More importantly, diabetes is the leading cause of nontraumatic leg amputations in the United States [6]. While the incidences of diabetic ulcers are sharply on the rise, pressure ulcers in critical care and intensive care patients are also increasing. The prevalence of pressure ulcers within inpatient settings has been reported to be 22%, with as many as 50–80% acquired within the hospital [7]. Diabetic foot ulcers (DFUs) and pressure ulcers represent major sources of morbidity and their care a massive burden financially. Sen and colleagues argue that with the sharp increase in the incidence of diabetes and obesity and with the increasing need for wound care of our veterans, investigation into tissue regeneration in chronic wound repair is vital [4].

Five phases for wound healing is introduced: hemostasis, inflammation, cellular migration and proliferation, protein synthesis and wound contraction, and remodeling [8,9], Fig. 1 [8]. However, mainly only three phases, inflammatory, proliferative, and remodeling [1,2] are presented due to the overlap of phases. These dynamic phases are associated with considerable complexity that involves soluble mediators, extracellular matrix (ECM) formation, and parenchymal cell migration [2]. The primary objectives of wound healing involve timely wound closure, prompt pain relief, and an aesthetically acceptable scar. Recent advances in wound healing research have markedly improved our understanding of the processes implicated in tissue repair and regeneration.

In this review, we focus on current treatment methods and potential future treatments based on growth factors and cytokines, small molecules, and stem cells. In addition, we describe potential early detection and management of wound microenvironment using sensor technology.

2. Current standard care

2.1. Acute and chronic wounds

There are generally two major classes of wounds: chronic and acute. Acute wounds can be superficial involving both the epidermis and superficial dermis, or full thickness in which the subcutaneous layer is compromised [3]. Examples of acute wounds are surgical incisions, thermal wounds, abrasions, and lacerations with the major associated complication of each being infection. Acute wound healing is regulated by cytokines and growth factors released proximal to the wound [10]. The inflammatory phase associated with wound healing involves neutrophil, macrophage, and lymphocyte migration to the wound producing symptoms of inflammation that last for approximately 2 weeks [11]. As stated previously, wound healing involves several stages and at any point the process can come to a standstill leading to a potential dysfunction. If inflammation persists for months or years the wound becomes classified as chronic and can be associated with numerous pathological alterations including increased protease activity and infection [12]. The proliferative phase follows the inflammatory phase, and is characterized by new tissue formation, granulation and epithelial tissue formation (re-epithelialization) and restores the vascular network. Keratinocytes involve repairing the epidermal barrier while fibroblasts and endothelial cells are responsible for angiogenesis and ECM production. Remodeling phase involves reorganization and contraction of newly formed matrix and can last for several years [8,9,13,14].

Generally, acute wounds tend to heal within 3 weeks while chronic wounds tend to persist for a minimum of 3 months since the time of injury [3]. Chronic wounds can result by destructing all the layers in skin including epidermis, dermis, and underlying subcutaneous fat tissue.

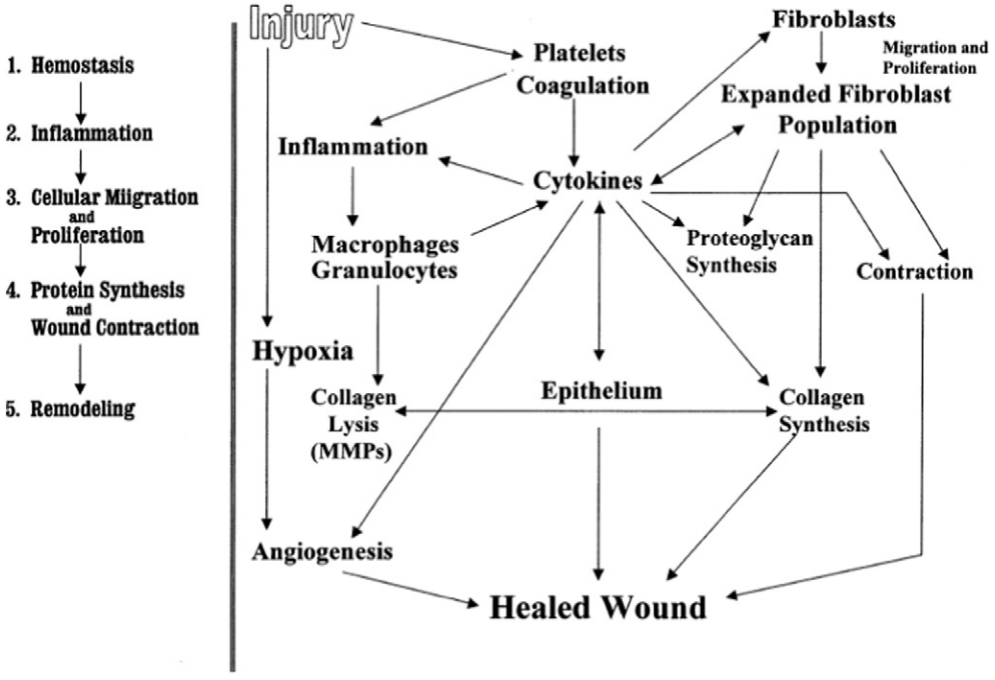

Fig. 1. The acute wound-healing cascade. The progression of acute wound healing from hemostasis to the final phases of remodeling is dependent on a complex interplay of varied acute wound-healing events. Cytokines play a central role in wound healing and serve as a central signal for various cell types and healing events [8].