

# WOUND HEALING: A Basic Overview and a New Approach

## WOUND HEALING: THE BACKGROUND

The principles of wound healing are based on four phases characterized by hemostasis, inflammation, proliferation, and remodeling.<sup>1</sup> Overall, wound healing is a complex process in which missing tissue layers and cellular structures are replaced and restored. Wounds occur for many reasons which include, but are not limited to trauma, burns, insect stings, vascular compromise, diabetes, or adverse effects of medications. To optimize the healing process, the underlying cause of a wound must be understood and controlled.<sup>1</sup>

## THE 4 PHASES OF WOUND HEALING

The first phase of wound healing is known as hemostasis, which occurs immediately post injury. The cells involved here are the platelets, whose main goal is to initiate clotting and prevent further blood loss.

Phase two is inflammation and this takes place during day one and up to day four post injury. Cells involved in phase two are neutrophils and macrophages, whose job it is to clean the site of injury via phagocytosis. This phase will present as erythema, swelling, warmth and with pain. The inflammatory response on the blood vessels cause the release of plasma and neutrophils into the surrounding tissue. The released neutrophils then digest bacteria and other debris in the area, helping to defend against the risk of infection. In addition to neutrophils, macrophages are also able to phagocytose bacteria, and they act as a second line of defense.

After phase two is complete, phase three also known as proliferation begins and lasts up until around day twenty-one in acute wounds.<sup>1,2</sup> The goal of phase three is to reestablish skin function and to close the wound. Clinically, phase three is characterized by angiogenesis, collagen disposition, granulation tissue formation, wound contraction, and epithelialization.<sup>2</sup> By the end of phase three the wound is closed, and the basic structure has been restored.

Lastly, phase four or remodeling (maturation) begins and can last up to two years. In this phase fibrocytes help remodel and realign the collagen tissue to produce greater tensile strength.<sup>2</sup>

## PAST VS. PRESENT

Although the mechanisms of wound healing have been constant and established, the approach to wound healing has changed greatly over the years. Wound care has evolved from magical potions, ointments and incantations to silicone gels and now to the effects of the microbiome.<sup>3</sup> The old approach to skin healing can be described as mechanical. Older therapies utilized silicone gels to act as a band-aid to cover the wound, rather than utilizing a scientific approach. Although silicone has been an effective therapy, researchers have found a more scientific approach. In the 1990s, wound healing was based on physio-chemical actions and started utilizing molecules such as sucralfate.<sup>4</sup> The thought behind this process was that sucralfate had both mechanical and chemical actions. It was not only mechanical, but also had a scientific pathway behind it. It could cover and protect the wound, but also attract water molecules and growth factors contained therein to repair wounds.<sup>4</sup>

## WOUND HEALING: LOOKING INTO TOMORROW'S APPROACH

Today, a more organic and natural approach has come to fruition due to the extensive research of the human microbiome. With over one hundred thousand billion bacteria, our microbiome, if measurable, would weigh about 2kg.<sup>5</sup> These recent studies have allowed researchers to see the positive association between the microbiome and various systems throughout our body. On average, our skin is renewed every twenty-one days. However, in the intestine where most bacterial species of the human microbiome are derived from, its epithelium is able to renew itself every four to five days.<sup>4</sup> Researchers saw this similarity and knew that there must be some sort of relationship between the intestine's healing process and its microflora.<sup>4</sup> Upon further studies, a correlation between the skin's microbiome and wound healing was established. It was found that epithelial cells are able to communicate with bacterial flora through Pattern Recognition Receptors (PRR) and Toll-Like Receptors (TLR). Specifically, TLR-5 is enhanced by a protein called flagellin. Upon the enhancement of this TLR-5 by flagellin, activation of growth factors that multiply on the surface of epithelial stem cells are expressed, which induces skin regeneration.<sup>4</sup>