How are you managing DFUs? Innovative Therapy in Accelerating Wound Healing

This is a brief summary of a presentation given at the annual fall conference of Wounds Canada, in Mississauga, Ontario, on November 16, 2017. It has been produced with the financial support of Acelity. The presenters were Christine A. Murphy, RN CETN(C) BSc(hons) MClScWH PHD, who leads a vascular limb salvage project in an acute care setting, with focus on innovative wound solutions for a challenging population; and Ken Unger, DPM FACFAS DABFS, whose areas of interest and expertise are reconstructive surgery of the foot and ankle, wound care and limb preservation in patients with diabetes.

Diabetic Foot Ulcers: An Overview

According to the Canadian Diabetes Association (2015), 3.4 million (9.3%) Canadians are living with diabetes. This number is expected to rise to 21.2% by 2025. One particular consequence of diabetes is diabetic foot ulcers (DFUs), which have a major medical, social and economic cost in Canada and around the world. Up to 25% of individuals with diabetes will have a DFU over the course of their lifetime. Following a below-the-knee amputation, the five-year mortality rate exceeds that of colon, breast and prostate cancer.

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Diabetic foot ulcers have a complicated and multifactorial etiology, including five main components:

- Peripheral neuropathy (loss of protective sensation)
- Structural changes of the feet
- Ankle equinus (tight posterior muscles)
- Soft tissue trauma: repetitive stress to tissue (callus), single event trauma, toenail disorders
- Peripheral vascular disease

DFU Treatment

When managing DFUs, health-care providers should focus on optimizing vascular supply, removing necrotic tissue, treating infection and choosing appropriate offloading and/or protection devices. Furthermore, in order to rebalance the wound-healing environment, special care should be taken to reduce microbial burden and biofilms, lower protease activity and maintain an appropriately moist wound environment.

Proteases and DFU Healing

One sometimes-neglected piece of the DFU-healing puzzle is the effect of proteases on wound healing. Proteases are enzymes that perform proteolysis, through which proteins are broken down into smaller polypeptides or amino acids. Are they perplexing, confusing, relevant, interesting? Do they affect healing outcomes? Do you think about them while you do your assessments?

Currently, the health-care sector is spending vast amounts of money on managing and treating chronic wounds. DFUs alone are more expensive than the five most expensive types of cancer. Consider how much is spent annually on wounds that are stalled. If this is such a problem, we must ask why it is still happening. One reason has to do with proteases: 90% of chronic wounds with elevated protease levels won't heal.

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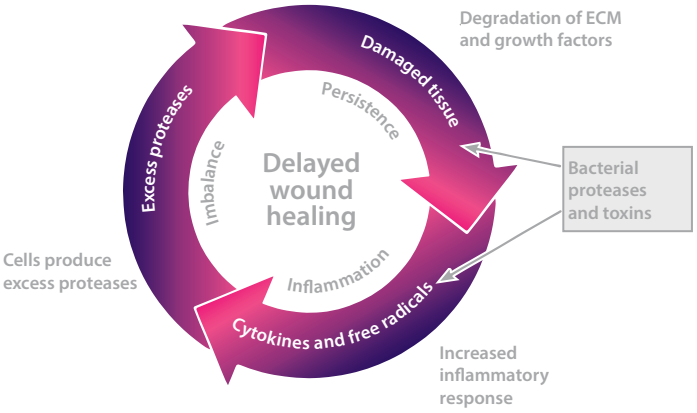
Steps of Wound Healing

Health-care professionals must support the body's tissue to let the body heal itself. In normal wound healing, four steps occur sequentially: hemostasis, inflammation, proliferation, and, finally, remodeling. A goal of wound healing is to regenerate a functioning group of cells, adhered to a stable extracellular matrix base, while closing the defect to prevent pathogen entry.

But what about when things go wrong? Often, chronic wounds get stuck in the inflammatory stage (see Figure 1).

Figure 1. Cycle of Delayed Wound Healing[1]



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Effect of Proteases on Chronic Wounds

Bacteria use proteases to invade the host. When a large number of proteases are present in a wound, the inflammatory response increases. This increased inflammatory response, in turn, promotes the production of even more proteases and the degradation of the extracellular matrix, which then causes additional inflammation. This cycle continues, resulting in a wound that has stalled in the healing cycle. Protease imbalance is implicated in many forms of diseases, including aneurysms and various types of cancer.

Several different types of proteases affect chronic wounds. The two main families are matrix metalloproteinases (MMPs) and human neutrophil elastase (HNE). When the MMP and HNE families of proteases are combined, all soft tissues in the wound are degraded—and healing stalls.

Management Strategies

How do you know if there is an elevated protease problem? If the DFU healing has stalled, it is time to take a closer look. Some signs of protease imbalance include poor quality granulation tissue, increased drainage, a cliff edge not moving forward (rolled edge appearance) and poor new blood vessel growth.

Certain types of dressings can help when protease imbalances are present. Dressings, when chosen correctly for the patient, can help with moisture balance, pH balance (bacteria like high pH), reduction of inflammatory proteases and the stimulation of a positive wound response by providing the components for building an extracellular matrix scaffold.

ORC/Collagen Dressings

ORC/collagen dressings have three main components: native collagen, denatured (broken) collagen and oxidized regenerated cellulose (ORC). Native collagen sequesters excess MMPs by acting as a decoy, and provides structure for neocapillaries, GF protection and cell attachment. Denatured collagen attracts cytokines, GFs and fibroblasts. ORC binds elastase (necessary for pro-MMPs to convert to active MMPs), binds metal ions such as zinc and calcium, binds free radicals and reduces pH.

Cellulose is extremely abundant in the world: it comes from wood pulp and cotton. The oxidization process makes it biodegradable. Cellulose is a hemostat (i.e. it stops bleeding), and it lowers pH, which makes the environment less bacteria-friendly. Cellulose also breaks down sugars to provide a source of energy and nutrients. *In-vitro* studies show that it increases cell growth, protects growth factors from degradation and inactivates protease activity.

When ORC and collagen are used together in a dressing with the correct ratio, a 100% reduction in elastase, a type of protease, is possible. This combination is also effective against bacterial proteases.

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In Summary

Diabetic foot ulcers are an ever-growing concern in Canada and abroad. One sometimes-overlooked factor in DFU healing is the role of proteases. When assessing and treating DFUs, consider whether proteases are a factor in stalled healing, and consider using a dressing that can help neutralize this contributing factor.

References

1. Gibson D, Cullen B, Legerstee R, Harding KG, Schultz G. MMPs Made Easy. Wounds International 2009;1(1). Available from: www.woundsinternational.com/media/issues/61/files/content_21.pdf.

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