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Advances in wound healing: an overview

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INTRODUCTION

Acute wounds normally heal in a very orderly and efficient manner characterized by four distinct, but overlapping phases: *hemostasis*, *inflammation*, *proliferation* and *remodeling*. Specific biological markers characterize healing of acute wounds. Likewise, unique biologic markers also characterize pathologic responses resulting in fibrosis and chronic non-healing ulcers.

The normal healing response begins the moment the tissue is injured. As the blood components spill into the site of injury, the platelets come into contact with exposed collagen and other elements of the extracellular matrix. This contact triggers the platelets to release clotting factors as well as essential growth factors and cytokines such as platelet-derived growth factor (PDGF) and transforming growth factor beta (TGF-ß). Following *hemostasis*, the neutrophils then enter the wound site and begin the critical task of phagocytosis to remove foreign materials, bacteria and damaged tissue. As part of this *inflammatory* phase, the macrophages appear and continue the process of phagocytosis as well as releasing more PDGF and TGFß. Once the wound site is cleaned out, fibroblasts migrate in to begin the *proliferative* phase and deposit new extracellular matrix. The new collagen matrix then becomes cross-linked and organized during the final *remodeling* phase. In order for this efficient and highly controlled repair process to take place, there are numerous cell-signaling events that are required.

In pathologic conditions such as non-healing pressure ulcers, this efficient and orderly process is lost and the ulcers are locked into a state of chronic inflammation characterized by abundant neutrophil infiltration with associated reactive oxygen species and destructive enzymes. Healing proceeds only after the inflammation is controlled. On the opposite end of the spectrum, fibrosis is characterized by excessive matrix deposition and reduced remodeling. Often fibrotic lesions are associated with increased densities of mast cells. By understanding the functional relationships of these biological processes of normal compared to abnormal wound healing, hopefully new strategies can be designed to treat the pathological conditions.

TREATMENT STRATEGIES

Revolutionary advances using tissue engineering, growth factors, animal fetal cell research, stem cell research, and gene therapy may offer new hope to patients who experience acute and chronic wounds.

According to the recent market scenario report, chronic wound care is estimated to cost $6 to $24 billion each year, about 5% of the total annual spending on Medicare and Medicaid combined. This is a worldwide problem, as Japan, Italy, Germany, the European Union, and the United States all have populations with greater than 20% of individuals over the age of 65. This age group is anticipated to double over the next 30 years. Several advances that are helping patients today and research that holds promise for tomorrow, including the following:

1) Tissue engineering

Tissue engineering allows physicians to treat tissue loss using minimal donor tissue. Advances such as multilayer membranes, transplantable sheets of living keratinous tissue, biodegradable polymers for cell transplantation, and tissue equivalents help improve the lives of patients today. Further research will continue to offer advancements in this area.

2) Scar prevention

Current treatment to heal scars focuses on silicone gel sheeting, which is easy to use, painless, and safe. Prior to this, very little was available to improve scars. Recently, significant strides have been made in understanding the mechanisms of scarring and the potential of the growth factorTGF-13 in blocking collagen synthesis.

3) Growth factors

Growth factors increase the wound's capacity to heal by causing cells to grow and attracting new cells to the wound. The use of growth factors to accelerate the healing of wounds offers tremendous promise as a therapeutic approach to treating chronic wounds such as diabetic ulcers and pressure ulcers.

4) Animal fetal cell research

Fetal wound repair, unlike adult wound repair, occurs with little or no acute inflammation or scarring. Animal-derived fetal cells are being studied for their value in regenerating damaged tissue resulting from acute and chronic wounds. Ongoing research in this area will focus on discovery of the fetal wound healing genotype for broad therapeutic application in wound repair. Research has identified stem cells as powerful regenerative tools in wound healing. These cells are already present throughout the body, including in bone marrow, muscle, and cartilage. Continued stem cell research will further define the role of these vital cells in wound repair. For example, potential exists to genetically manipulate stem cells to correct inborn errors of metabolism or to deliver gene products as medicine.

5) Gene therapy

Gene therapy in wound healing is useful as a delivery mechanism to provide proteins directly into the cells of a wound to promote healing.

Final Facts

Unless we focus on solutions now, chronic wounds will become a demographic time bomb as the population ages. As we continue to develop new information about the unique biological markers associated with normal and pathologic wound healing responses, the better prepared we will be to develop new strategies to treat these costly clinical problems. In addition, understanding this basic biological information will allow wound care specialists greater insight into the importance of how their skills can impact the healing response.