
Wound Healing: An Introductory Clinical Approach

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EDITOR'S NOTE

In this article, the authors provide a comprehensive dialogue concerning an important topic for the primary care physician. Consistent with the charter of this publication, the article's information and structure invite the reader to keep it as a ready reference. The authors conclude that new wound healing innovations are in development, so look for more information in future issues of The Contemporary Podiatric Physician.

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INTRODUCTION

Wound Healing has become the "buzz word" of the '90's. Podiatric physicians must be prepared to master and to clinically apply this rapidly advancing technology.

The intent of this article is to present an introductory clinically simplified review of wound healing with a brief discussion of commonly used products purporting to aid the healing process.

The practice of podiatric medicine includes the management of a wide variety of wounds. Whether the defect is a surgical incision, a traumatic disruption of the skin, or management of ulcers, the podiatric physician must have a basic understanding of wound healing in order to provide an optimal environment for healing these defects.

WOUND CLOSURE

The goal of the physician, in wound healing, is elimination of the void or defect. Clean surgical incisions or traumatic lacerations are ordinarily closed by suturing to approximately the wound edges.

Grossly contaminated wounds and ulcerations are usually treated open. Open treatment of wounds permits necrotic fragments, infecting agents, and foreign debris to exit the wound. It also enhances oxygenation of injured tissues to prevent anaerobic infections.

Three types of wound closures are normally utilized: Primary, Delayed Primary, and Secondary.

PRIMARY WOUND CLOSURE

Primary wound closure is the method of choice for clean surgical wounds and lacerations in which the skin margins are amenable to closure. The wound must be considered to be free of gross contamination, infection, nonviable tissue, and foreign bodies.

Primary closure is contraindicated in: crush wounds, mutilated wounds, high impact wounds, or dirty wounds.

Primary wound closure results in the least scar formation and is performed using sutures, staples, or steri strips®.

DELAYED PRIMARY CLOSURE (DPC)

Delayed Primary Closure is employed in grossly contaminated or infected wounds or following incision and drainage. The DPC technique requires complete debridement of all necrotic or nonviable tissue, copious irrigation, and loosely packing the open wound to permit drainage of purulent materials. Tight wound packing only fosters more necrosis of wound tissues and infection. After three to five days when negative wound cultures are obtained and the wound appears clean, the defect is then closed primarily by tying the untied sutures that were placed across the wound edges at the initial surgical debridement.

SECONDARY WOUND CLOSURE

Secondary wound closure is used in wounds that can not be closed by primary or delayed primary closure. These wounds are often grossly contaminated, infected, or the wound edges cannot be approximated as may be the case in many ulcers. Secondary wound closure requires debridement of nonviable tissue, daily wound care, and appropriate antibiotics. Healing in this situation follows the same process as all wounds. Wound closure occurs by contraction involving the centripetal movement of the whole thickness of the surrounding skin, including the dermis.¹ Through this process the wound defect is filled by granulation and epithelialization.

PHASES OF WOUND HEALING

In all three wound closure techniques the phases of wound healing are the same, however, the time spent in each phase will vary depending upon the method of closure indicated.

Wound healing begins immediately after the tissues are violated, such as in laceration, surgical incision, or ulceration.

Basically, wound healing is divided into three phases: the Substrate (or Inflammatory) Phase, the Proliferative (or Fibroblastic) Phase, and the Remodeling Phase.

SUBSTRATE PHASE: DAY 1 TO DAY 4

The substrate phase, also known as the inflammatory, or lag phase begins at the instant of trauma to the skin. It lasts from one to four days. The duration of this phase is dependent upon the extent of trauma to the adjacent and underlying tissues. A direct relationship exists between the extent of tissue trauma and the increased time elapsed in this phase. The time elapsed in this phase influences how severely the wound will scar. This time period does not pertain to delayed primary or secondary wound closure. The same processes occur, however, the one to four day time does not occur because the surgical debridement will perpetuate the inflammatory, vascular, and cellular responses.

An immediate local vascular response occurs upon wounding the skin. Within the first few minutes, vasoconstriction limits blood loss and aids in leukocyte adherence to the vascular bed.² Active vasodilation then follows. Polymorphonucleocytes (PMN's) are the first cells to migrate in and accumulate because of their abundance in the vascular system.

The PMN's assist in forming the exudate, which is a viscous fluid composed of PMN's, leukocytes, and fluid from local vessels.

Later the PMN's begin to die and are lysed forming a transudate. The transudate consists of dead degenerated

PMN cellular components, which make the exiting fluid less viscous.

Histamine, serotonin, heparin, leukotaxime, and several hydrolytic enzymes are released from the mast cells into the area.³ Heparin acts as an anticoagulant and serotonin as a vasoconstrictor. Histamine increases the permeability of post capillary venules resulting in plasma protein leakage and stimulation of leukocyte diapedesis.³

In the substrate phase there is no initial fiber deposition to aid in wound strength, however, its function is removal of necrotic debris in preparation for collagen deposition.¹

Hemostasis is achieved in this phase by platelet aggregation that forms a plug which fibrin is deposited in later. This is an attempt by the body to keep the site sterile. Inflammation that occurs in this stage is critical to fibroplasia. Excessive inflammation leads to increased fibroplasia resulting in hypertrophic scar or possibly a keloid.

PROLIFERATIVE PHASE: DAY 4 TO DAY 20

The proliferative or fibroblastic phase begins about the fourth day and continues until approximately the twentieth day in primary wound healing. In delayed primary and secondary wound healing, this phase lasts until granulation and epithelialization is complete.

The proliferative phase consists of: epithelialization, contraction of the wound, and connective tissue repair.¹

Epithelialization occurs through contact enzymatic guidance. It is inhibited through cell to cell enzymatic contact in which the epithelial cells stop migrating.

Connective tissue repair occurring in the proliferative phase greatly adds to wound strength. *Wound tensile strength* is achieved by the fibroblasts laying down collagen. The fibroblasts remodel the wound, then disappear as they differentiate into collagen. Collagen mucopolysaccharide secretion contributes to fibrin orientation and polymerization, i.e. fiber building.⁴ Vitamins, particularly vitamin C, are important to wound tensile strength. Collagen formation continues up to sixty days in primary wound healing.

The way in which collagen is laid down is more important than the quantity of collagen in the healing wound. Collagen fiber alignment is best achieved when the skin edges are everted, permitting anatomic approximation.

New vascularization occurring in the proliferative phase enhances collagen formation by increasing oxygen tension at the site. The combination of new capillary formation and abundant fibroplasia results in the formation of granulation tissue. This granulation tissue fills the defect in secondary wound closure and continues until wound closure is achieved.

In the proliferative phase the tensile strength increases daily often permitting suture removal on the tenth to fourteenth day. At this time the tensile strength may be suffi-

cient to prevent dehiscence, but the wound is only at 25-30% of its original strength. Thus, external reinforcement is necessary to insure wound approximation. Plantar wounds require longer suture retention time.

REMODELING PHASE: DAY 21 TO 1 YEAR

The remodeling phase is the final phase of wound healing. It occurs from about day twenty-one up to one year after injury in primary wound healing.

In the remodeling phase the collagen fibers that have been laid down, begin to arrange themselves for maximum tensile strength.⁴ After approximately one hundred days the tensile strength will not increase unless stress occurs across the wound site.

Wound stress via normal ambulation, or physical therapy will favorably increase wound strength in the remodeling phase.

TOPICAL AGENTS IN WOUND CARE

Topical agents are routinely used in the management of both acute and chronic wounds, including ulcers. These preparations have a negative effect on wound healing when improperly used.

The clinical rationale behind many solutions or preparations used today is perhaps based on tradition rather than scientific fact.

Antiseptic solutions (not antibiotic) are commonly used in an attempt to promote healing, however, research questions the concentration used and the effectiveness of some of these agents. Traditionally, various antiseptic solutions were used for wound irrigation and/or applied to dressings attempting to reduce bacterial contamination and subsequent growth. Concentrations of antiseptic solutions used in wound care must not exceed the minimum concentration required to retain its bactericidal effectiveness and must not be cytotoxic to regenerating tissues.

Some examples of topical solutions are: Povidone-iodine, Dakin's Solution, Hydrogen Peroxide, Acetic Acid, or Physiologic Saline or Ringers Solution.

POVIDONE-IODINE

Povidone-iodine, essentially free iodine bound to polymer polyvinyl-pyrrolidone (an iodophor), is perhaps the most traditionally used topical antiseptic to date. This agent is used erroneously as an irrigant, dressing solution, or direct topical agent.

Current research reports povidone-iodine's deleterious effects on wound epithelialization and fibroplasia when used at non-diluted concentrations. This iodophor has been shown to be bactericidal against staphylococcus aureus, however, the wisdom of its use as a wound healing

agent is questioned because of its adverse effects on tensile strength and its cytotoxicity.⁷

Lineaweaver and associates⁸ noted that povidone-iodine diluted to a 0.001 percent concentration is bactericidal to staphylococcus aureus, yet non-cytotoxic to cultured human fibroblasts. It is also noted that povidone-iodine can be absorbed into the circulation and possibly affect renal function with prolonged use.⁶

Even though iodine is an active antiseptic agent when released from solution, *povidone-iodine is readily inactivated by binding to serum proteins as in exudating wounds.*⁹

*Povidone-iodine is ineffective when applied to a wound colonized with greater than 10 to the 5th power organisms per gram of tissue.*⁵

Any povidone-iodine agent must be greatly diluted before irrigating or placing on a wound or ulcer site.

DAKIN'S SOLUTION

Dakin's Solution is a dilute neutral 0.5% Na hypochlorite and 0.4% Boric acid solution, commonly used for cleansing and reducing bacterial concentrations (not sterilizing) in wounds.

Dakin's Solution is bactericidal against streptococci, staphylococci, and pyococcus micro-organisms; however, it is toxic to granulation tissue and fibroblasts.^{5,6} Studies also reveal that Dakin's retards collagen synthesis and delays epithelialization.⁶ Dakin's Solution inhibited 90% of neutrophil migration into a wound, thus undermining the body's natural defense system.⁶

The author's clinical experience indicates that Dakin's Solution wound healing inhibitory effects can be used to an advantage in 50% concentration for treatment of pyogenic granuloma's. The physician must first be sure the mass is a pyogenic granuloma.

HYDROGEN PEROXIDE SOLUTION

Hydrogen peroxide, by its effervescent action, is a mechanical cleansing agent and a non-selective debriding agent.⁵ Hydrogen peroxide is primarily indicated for loosening dried exudate or debris including healthy regenerating tissue.⁶

Research shows hydrogen peroxide disrupts new capillaries in granulation tissue.⁶ It also oxidizes wound debris and is toxic to fibroblasts in healthy healing tissue.⁵

Clinically, hydrogen peroxide may cause the formation of subcutaneous gas in deep tunneling wounds, particularly in diabetics. *Subcutaneous bubbling may be noted in smaller quantities on x-ray much the same as gas produced by anaerobic organisms. Anaerobically produced gas may be observed in larger quantities. Palpation often reveals the presence of subcutaneous gas by the feel and/or sound of "crackling" in the underlying tissues.*

ACETIC ACID

A 0.5% acetic acid irrigation solution is effective for clearing *Pseudomonas aeruginosa* from contaminated or infected wound beds. It is not bactericidal. Dilute acetic acid merely creates an acidic environment unfavorable to the growth of *Pseudomonas*.

Acetic acid irrigation is only an adjunct to appropriate drainage, antibiotics, and wound care. It does not solely constitute adequate treatment of *Pseudomonas* infections.

It is effective against saprophytic *Pseudomonas* wound inhabitation, but only in the absence of any signs of acute wound, regional, or systemic *Pseudomonas* infection.

Acetic acid is not effective against gram positive or other gram negative bacteria that may replace the vanquished *Pseudomonas* organisms.⁶

Acetic acid is, likewise, toxic to fibroblasts and impedes epithelialization necessary for wound healing.

PHYSIOLOGIC SALINE OR RINGERS SOLUTION

Either physiologic saline or Ringers Solution may be used to irrigate and/or provide a moist environment for wound healing. Neither exhibits bacteriostatic or bactericidal properties other than dilution or washing away bacteria during irrigation. Both, however, provide an almost physiologic environment for the clean non-infected wound. Some surgeons prefer lactated Ringers Solution.

Wet-to-dry dressings are counterproductive in early wound healing unless the primary objective is "no touch" wound debridement.

DRESSING MATERIALS/COLLOIDS USED IN WOUND CARE

A variety of dressing materials have become available in recent years. Most claim to significantly hasten wound healing compared to the more traditional wound care; i.e. soaks, debridement, or dressings.

The hydrocolloids, calcium-sodium alginates, and growth factors; indications and contraindications are clinically discussed.

HYDROCOLLOID DRESSINGS

Hydrocolloid dressings contain hydroactive and absorptive particles incorporated into a polyurethane type material or substance. This substance possesses absorptive properties while maintaining a moist environment in and for the wound.

The surface base material is waterproof and impermeable to bacteria simultaneously permitting high oxygen and

water vapor permeability thus preventing skin maceration and secondary infection. The dressing interacts with the moisture of the wound forming a soft almost gelatinous-like mass on the undersurface of the hydrocolloid dressing.

When the dressing is removed, the wound is debrided with little or no injury to the newly formed wound granulation.

Dressing material flexibility and adhesive margins contribute to ease of application at a variety of wound sites. Hydrocolloid dressings are also manufactured in varying thicknesses. Occasionally their transparent nature provides for simpler wound inspection.

Hydrocolloid dressings are indicated for: partial thickness wounds, shallow full thickness wounds, second degree burns, venous stasis ulcers, stage I-II decubitus ulcers, and certain post-op wounds.

They are designed to manage superficial dry-to-slightly exuding dermal ulcers.

Hydrocolloid dressings are specifically contraindicated in dermal ulcers involving: muscle, tendon or bone; third degree burns, any wound with clinical signs of infection — Tuberculosis, Syphilis or Deep Fungal Infection.^{10,11}

CALCIUM-SODIUM ALGINATE FIBER WOUND DRESSINGS

The alginates are naturally occurring polysaccharides found only in brown seaweed. Alginate products have been available for several years, but have only recently gained popularity as being more cost effective in management of ulcers.

Alginate materials are highly absorbent, easy to apply, and are virtually painless upon removal. The alginate fibers absorb wound exudate and form a gel/fiber matrix. This matrix provides warm, moist environment to promote wound healing.

The alginates are indicated in: clean diabetic ulcers, pressure sores, venous stasis ulcers, arterial insufficiency ulcers, first and second degree burns and certain post-op incisions.

Since alginate dressings are non-occlusive, they may be used in infected wounds, but only in conjunction with appropriate antibiotic and debridement therapy. Alginate dressings must be changed at least once daily in the presence of infection.^{12,13}

The alginates are contraindicated in full thickness wounds involving: muscle, tendon, bone or third degree burns.¹³

GROWTH FACTORS

A promising new concept that may show promise in the future has recently begun clinical trials.

Platelet Derived Wound Healing Formula (PDWHF) is commercially marketed as "Procuran"® by Cura Tech Inc., Stony Brook, New York. Other related products by different commercial laboratories are also becoming available for clinical trial.

PDWHF is designed for use in conjunction with other wound management techniques (such as debridement, vascular work-up, and appropriate antibiotics etc.) thus, forming an optimal treatment regimen aimed at promoting positive wound healing.¹⁴

PDWHF solution is derived from the patient's own blood. Sixty milliliters of blood is drawn and sent to a processing laboratory where the platelets are selectively removed and the growth factors are extracted.

The growth factors are made into a sustaining solution and are dispensed in single use tubes. Enough growth factor for 10 weeks of treatment is extracted from one 60 ml blood sample. The tubes of processed PDWHF are kept frozen until just before application to the wound site. A growth factor regimen is used for about 10 weeks of treatment.

Patients apply Procuran® by saturating gauze and lightly packing into the open wound area(s). The wound is then covered with a non-adhesive petroleum impregnated gauze to prevent drying. The site is covered with an appropriate dressing. This dressing is changed every 12 hours and normal saline or triple antibiotic solution is applied.

The initial results of growth factor trials appears to be promising.

CONCLUSION

It appears that newer wound healing innovations are in development by both domestic and foreign laboratories. We can assume that in the reasonably near future, wound healing technology will advance to such a state that our current technology will be of historical interest only.

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