GETTING TO GRANULATION: EFFECTIVE MANAGEMENT OF THE CHALLENGING OPEN WOUND

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As a clinician, your objectives when faced with a wound are like those of the white blood cell: to rid the wound of contamination and necrotic tissue and to provide an environment that promotes granulation. These objectives are best achieved by combining knowledge of the body's own wound healing processes with accurate assessment of tissue viability, proper lavage, surgical and/or autolytic debridement, and moist wound management.

WOUND HEALING FUNDAMENTALS

The inflammatory/debridement phase typically occurs over the first 3 to 5 days after wounding. White blood cells are attracted into the wound by substances released by platelets and leukocytes already in the wound, injured endothelium, damaged tissue, bacteria, and foreign material. White blood cells provide *selective, autolytic debridement* of bacteria, foreign material, and necrotic tissue by phagocytosis and secretion of proteolytic enzymes. This debridement is selective because only injured or dead cells and damaged matrix are removed; healthy tissue is spared. The strength of the wounded tissue decreases during this phase because tissues are being removed and the repair process has not yet begun. As autolytic debridement is completed, cytokines produced by macrophages stimulate the repair phase of healing.

Granulation, epithelialization, and contraction make up the repair phase, which lasts for 2 to 4 weeks. Granulation tissue consists of the vessels and matrix produced by fibroblasts and endothelial cells as they migrate into the debrided wound. Granulation tissue forms at a rate of ~0.4 to 1.0 mm/day, and it must be in place before epithelialization and contraction can occur. Epithelial cells migrate out onto the granulation tissue, which provides the oxygen, moisture, and surface they require to create a new epidermis. The rate of epithelialization can be up to several millimeters per day. Wound contraction occurs when the fibroblasts which have created the granulation tissue meet in the center of the wound and develop smooth muscle-like characteristics. These myofibroblasts are linked to each other by intercellular connections and linked to the wound edges via their attachments to the granulation tissue. Contraction of the myofibroblasts exerts a centripetal force on the skin edges, drawing them toward the center of the wound. Thus, during the repair phase, skin coverage of the wound is achieved in two simultaneous yet independent means: epithelialization (builds new skin) and contraction (pulls pre-existing skin over the wound).

During the remodeling phase, which continues for months to years, collagen production and destruction reach equilibrium. Collagen aligned along lines of force becomes bundled into

larger fibers and cross-linked, adding to tissue strength. Collagen that is randomly oriented is exposed to collagenases and lysed.

Each phase of wound healing sets the stage for the phase that follows. Thus, the wound must spend time in all 3 phases in order for full healing to occur.

LAVAGE

Properly done, lavage removes foreign material, decreases bacterial counts, rehydrates tissues, and speeds healing. Improperly done, lavage can damage tissue, delay healing, and increase the risk of infection. Fluid pressure, volume, flow, and antiseptic concentration are variables the veterinarian can manipulate to maximize efficacy and safety of lavage.

The lavage pressure needed to remove microscopic particles and bacteria is higher than that required to remove gross debris. Thus, just because a wound looks clean does not mean that lavage has been adequate. The lavage pressure which maximizes removal of debris and bacteria while minimizing tissue damage is 7 – 8 psi. Bulb syringes, squirt bottles, and syringes without needles do *not* provide adequate lavage! For example, a liter plastic bottle of saline with holes poked in the top with a needle only generates 2 – 4 psi. On the other hand, a 35 cc syringe with a 16-22 g needle generates 15-18 psi, which is too high. The 'just right' level of 7-8 psi is most accurately achieved via a needle (16 to 22 g) on a standard intravenous drip set attached to a 1 liter bag of fluids pressurized to 300 mm Hg with an emergency pressure sleeve.

While contamination decreases as lavage volume increases, large volume does not compensate for inadequate pressure. Sedation and analgesia are likely needed when lavage is done with appropriate pressures. Delivering the lavage with a pulsatile action removes bacteria more effectively than a continuous flow (continuous flow is a drawback of the liter bag delivery system).

Tap water is okay for removing gross contamination in the initial lavage of severely contaminated wounds. However, because it is cytotoxic to fibroblasts and because a spray hose off the sink is not likely to provide the appropriate pressure, tap water lavage should be followed by lavage with a sterile, non-toxic solution applied at the proper pressure, such as normal saline, 0.05% chlorhexidine solution (e.g. 25 ml of 2% chlorhexidine + 975 ml of diluents), or 0.1% - 1% povidone-iodine solution (e.g. 10 ml of 10% P-I + 990 ml diluents for 0.1%; 100 ml of 10% P-I + 900 ml diluents for 1%). Higher concentrations may delay epithelialization and or contraction, while lower concentrations may not be antimicrobial. Dilution by eye based on the color of the solution is not recommended as the actual concentration achieved may be inappropriate. It is important to use the solution, not the scrub, formulation of these antiseptics as the detergent in the scrub is harmful to the non-skin tissues.

ASSESSMENT OF TISSUE VIABILITY

Attachment, color, and texture appear to be most reliable means of assessing tissue viability. Tissues that are unattached have clearly lost their blood supply and are no longer viable. The viability of the distal portion of a tissue flap that exceeds a length to base ratio greater than 2:1 or 3:2 may be poor. The color of necrotic tissue varies from black to brown to yellow to grey as the moisture content increases. Texture also varies with moisture content: desiccated necrotic tissue becomes firm and leathery and persists as an eschar, while moist

necrotic tissues are selectively broken down by leukocyte proteases, producing slough, a yellow or grey, wet, stringy substance (like mozzarella cheese on a pizza). Slough impairs healing and should be removed. It must be distinguished from a fibrin coating, which is yellow and gelatinous (as in grilled cheese). Fibrin can be left in place as it does not impair healing (and attempts to remove it may). Inflammatory exudate (pus) is wound fluid containing leukocytes (especially degenerating neutrophils) and dead tissue. Recognize that slough, fibrin, and pus do not mean that the wound is infected.

Cold temperature and absence of bleeding can indicate lack of viability or may just be due to transient vasoconstriction, hypovolemia, and/or hypothermia associated with trauma. Thus, these conditions should be corrected before making a decision based on temperature or lack of bleeding. Bright red flowing blood from a cut edge is a good sign of viability; dark, oozing venous blood indicates congestion and poor perfusion. Absence of sensation is not a clear sign of non-viability, since feeling may be altered by inflammation or treatment with analgesics or sedatives, and also because tissues can be viable in the absence of innervation.

DEBRIDEMENT:

Debridement is the process of removing dead or damaged tissue and foreign material from a wound. It promotes healing by eliminating physical barriers to granulation and epithelialization, removing a media for bacteria, decreasing exudate production, releasing inflammatory mediators that promote healing, and improving the clinician's ability to assess the wound. A combination of debridement methods is typically employed in wound care, and a given wound may require debridement multiple times.

MECHANICAL DEBRIDEMENT - SURGICAL

Surgery is one form of mechanical debridement. It is selective within the surgeon's ability to distinguish between viable and nonviable tissue (see above). Techniques range from the conservative resection of clearly devitalized (and thus insensate) surface tissue in an awake patient to aggressive resection of deeper devitalized tissue in an anesthetized patient in the operating room. Regardless of the approach, the wound should be prepared as for any surgical procedure, with proper clipping and cleaning of the peri-wound area, lavage of the wound, and the use of sterile instruments, gloves, and aseptic technique. In unstable patients, aggressive surgical debridement will typically be performed after optimization of the patient's cardiovascular, respiratory, and metabolic systems (to the extent that these changes are not caused by the wound itself). This delay also gives tissues some time to 'declare' as viable or non-viable; most will declare within 24 hours of injury. Moist wound healing techniques (see below) can be used to start autolytic debridement in a patient that is too unstable for surgical debridement.

A layered approach to surgical debridement is useful, removing each subsequent layer of necrotic or devitalized tissue until viable tissue is reached. The wound should be explored as well, identifying the status of key anatomic structures, opening pockets of dead space, and removing deeply imbedded foreign material. Tissue that is clearly necrotic must be removed, as its presence only delays healing and increase the risk of infection. Large amount of muscles and other organs (50% lung, 70% small intestine, 75% liver, 100% spleen) can be removed, and

many large vessels (e.g. both carotid arteries, both jugular veins, hepatic artery, femoral artery) can be ligated in dogs and still result in a good quality of life.

The following guidelines can be used in cases where the viability of a given piece of tissue is unclear. “When in doubt, cut it out” if there is only one opportunity to access that tissue, there is plenty or residual tissue so it won’t be missed, and/or consequences of later necrosis are severe. Examples include damaged muscle deep in a wound or damaged tissues inside the abdomen or thorax. On the other hand, “When in doubt, if it’s skin, leave it in” if there will be multiple opportunities to assess the tissue, the tissue is needed for later closure, and consequences of later necrosis are not severe because the tissue can be readily removed at that time. An example would be damaged skin on a distal limb, where there is not much redundant skin available and so you would like to have it for closure, and which can be easily reassessed without surgery during a bandage change.

If there is any question about whether all contamination or non-viable tissue has been removed, the wound should not be closed, or if closure is necessary, a drain should be placed. A bandage employing moist wound healing techniques provides the opportunity for ongoing autolytic selective debridement of the open wound (see below).

MECHANICAL DEBRIDEMENT – WET-TO-DRY

Wet-to-dry bandages, using gauze soaked in saline or antiseptic solution, mechanically debride wounds. Because gauze is absorptive and non-occlusive, wound exudate moves to the outer bandage layers where the moisture evaporates. Fibrin on the wound surface adheres to the gauze as drying occurs. When the dry dressing is removed, adherent tissue is pulled away as well. Wet-to-dry bandages are effective in removing necrotic tissue from the surface of a wound. However, a huge disadvantage of the wet-to-dry bandage is its lack of selectivity – i.e. both necrotic and viable tissues adhere to the dressing and *both* are removed when the dressing is changed, delaying healing. Additional disadvantages of the wet-to-dry technique include loss of white blood cells as they migrate into the open-weave dressing, ability of environmental bacteria to penetrate the gauze, aerosolization of bacteria as the dressing is removed, pain when worn and when removed, remnants of gauze fiber that stay in the wound and induce inflammation, and ultimately the higher cost of treatment due to the need for more frequent bandage changes (which also often require sedation) and longer healing times. Wet-to-dry bandages are no longer advocated by wound care experts in human medicine and are increasingly being replaced in veterinary medicine by moist wound healing practices that support autolytic debridement.

AUTOLYTIC DEBRIDEMENT

Autolytic debridement is carried out by white blood cells. As described above, it is a very selective means of debridement, sparing healthy tissue. The clinician can support autolytic selective debridement by applying a moisture retentive dressing (see below) that keeps the wound moist and warm, maximizing the activities of white blood cells and their proteases. Because no anesthesia or surgery is required, autolytic debridement is very safe, making it an excellent means of debridement in compromised patients. Moist wound healing techniques provides round-the-clock autolytic selective debridement.

MOIST WOUND HEALING

Moist wound healing (MWH) maximizes the body's own healing mechanisms by maintaining an appropriate level of moisture in the wound. MWH is standard in human medicine and increasingly replacing the wet-to-dry or dry bandage in veterinary medicine. Moisture retentive dressings (MRD) and negative pressure wound therapy are two means of supporting MWH. Advantages of moist wound healing include selective autolytic debridement, accelerated granulation, epithelialization, and contraction, prevention of infection, increased patient comfort, and decreased cost of wound management.

Moist wound healing supports *selective, autolytic debridement* of bacteria, foreign material, and necrotic tissue courtesy of the white blood cells and the proteases they secrete. This process is selective because only injured or dead cells and damaged matrix are removed; healthy tissue is spared. As autolytic debridement is completed, cytokines produced by macrophages stimulate the repair phase of healing. The clinician can support autolytic selective debridement by applying a moisture retentive dressing that keeps an appropriate amount of wound fluid in the wound. The moisture and warmth under such a dressing maximizes the activities of white blood cells and their proteases, and the wound fluid contains a physiological ratio of proteases, protease inhibitors, growth factors, and cytokines appropriate to the current stage of wound healing. Moist wound healing also accelerates the repair phase (i.e. granulation, epithelialization, and contraction) and counters all of the disadvantages listed above for wet-to-dry dressings.

The infection rate under a MRD is no greater than, or significantly less than, the infection rate under gauze or non-adherent pads. While bacterial viability is supported by a moist wound environment, so too is the viability and function of the immune system, and the advantage appears to go the latter. Reasons for the anti-infective effect of a moist wound environment include increased efficacy of white blood cells and proteases, less desiccated tissue (which is a media for bacteria), lower oxygen tension and lower pH (which attract white blood cells, stimulate angiogenesis and collagen formation, and inhibit bacteria), sustained contact between systemic antibiotics in wound fluid and the wound, the barrier effect of MRD to exogenous bacteria, and less frequent need for bandage changes.

MOISTURE RETENTIVE DRESSINGS

Familiarity with the principles of moist wound healing and the variety of interactive MRDs now available allow the clinician to tailor the bandage to the needs of the wound at each stage of wound healing. While there are literally hundreds of MRDs on the market, a focus on 5 main dressing categories (calcium alginates, polyurethane foams, hydrocolloids, hydrogels, and polyurethane films) will allow the clinician to effectively apply MWH techniques to the vast majority of wounds (Table 1). To ensure the wound is bathed in the right amount of wound fluid (moist, not dry nor soaking wet), the MRD's absorptiveness is matched to the exudate level of the wound; for dry wounds, an MRD that adds moisture to the wound is selected. As for any wound, the dressing and tissue should be handled using aseptic technique.

Maceration occurs when wound fluid spills over onto the skin surrounding the wound, causing overhydration of the skin. Excoriation is damage to the skin caused by proteases in the

wound fluid, and is more likely in chronic wounds which contain high levels of matrix metalloproteinases. Both maceration and excoriation compromise the barrier function of the skin. They are prevented by keeping the moisture in the wound and not on the peri-wound skin. This is achieved by cutting the dressing to fit within the borders of the wound. An imprint of the wound can be made on the dressing to provide an outline of the wound for appropriate sizing. The dressing needs to be in contact with the wound bed, so the depth and contour of the wound should be taken into account when cutting the dressing to fit. For deep or highly contoured wounds, moisture retentive gels or powders can be employed instead of sheet dressings to ensure this contact is achieved.

The frequency of bandage changes depends on the amount of exudate produced and how well it is being handled by the MRD. During the inflammatory phase of healing when exudate production is highest, a properly absorptive MRD is typically changed every 2 to 3 days. As granulation tissue forms, a less absorptive dressing is typically in order, and the interval between bandage changes may be increased to 4 to 7 days. As for any type of bandage, bandage change should be done if strike-though occurs regardless of the timing.

Many MRDs combine with wound fluid to form a gel. It is normal for this gel to have a slight odor and yellow color, which can give the impression of infection. The wound and whole patient should be examined for signs of infection such as redness, swelling, pain, purulent discharge, fever, etc. In the absence of such signs, the bandage change can proceed as planned. If infection is present, MWH should still be used to maximize white blood cell function. In the presence of infection, MRDs may need to be changed more often.

It is also normal for new epithelial tissue to appear white instead of pink under a MRD. This tissue should pink-up in a few days. Persistence of the white color suggests maceration, indicating too much moisture. The clinician should then select a MRD that will better handle the exudate in the wound or add less moisture to the wound.

Wounds with a lot of damaged tissue may appear to get larger initially under an MRD. This is because the white blood cells are doing their job of removing damaged tissue during the inflammatory/debridement phase. The healthy tissue that remains will be the source of cells used in the repair phase of wound healing.

See Table 1 for information on the properties, indications, and contraindications of common moisture retentive dressings.

NEGATIVE PRESSURE WOUND THERAPY

With negative pressure wound therapy (NPWT), sub-atmospheric pressure of -75 to -125 mm Hg is applied to the wound through a dressing. The vacuum continually pulls fluid through the wound to maintain a moist environment. On the gross level (macrostrain), the vacuum draws the wound edges together, removes excess exudate, and decreases tissue edema, thus improving perfusion and lymphatic flow. On the microscopic level (microstrain), the negative pressure stretches cells, which in turn stimulates them to proliferate and migrate as needed for wound healing. NPWT results in acceleration of granulation tissue formation and ultimately of wound healing.

NPWT may be applied for one day or several weeks depending on the wound, with a dressing change every 2 to 3 days. Application of the vacuum in an intermittent fashion (5 minutes on, 2 minutes off) appears to be more advantageous than a continuous vacuum – this

may be because of the repeated effects of microstrain as the vacuum turns on and off. Commercial units allow precise control of vacuum strength and timing and convenient collection of exudate. They employ special-density polyurethane foam (different from the polyurethane dressing discussed above) that is placed in contact with the wound. A fenestrated pad is placed on the foam and attached via a tube to a collection device on the unit. The wound, foam, and pad are sealed from the outside environment with transparent adhesive sheets.

NPWT is used on acute and chronic wounds, skin grafts, skin flaps, dehisced incisions, and closed surgical incisions, with the goals of stimulating granulation tissue formation and managing edema and/or exudate. Contraindications for NPWT include neoplasia, coagulopathy, and periwound tissue that is too unhealthy for the application of the adhesive drape.

References available on request.

Table 1. Characteristics of Common Moisture Retentive Dressings

MRD	Exudate Level	Properties	Indications	Contraindications
Calcium Alginate	High Absorbs 20-30 times its weight.	Made from seaweed Felt-like material that turns to gel as absorbs wound fluid.	Especially good for autolytic debridement of contaminated, moderate to highly exudative wounds. Good stimulator of granulation tissue. Hemostatic.	If insufficient exudate, will not gel and can dehydrate wound.
Polyurethane Foam	High	Soft foam; does not gel.	Good for autolytic debridement, stimulation of granulation, and stimulation of epithelialization. Can wick moisture out of macerated skin. Pre-moisten to soften eschar.	Insufficient exudate. Foam is too soft to provide protection to boney prominences.
Hydrocolloid	Low to moderate	Sheet, paste, or powdered forms all turn into a gel as absorbs wound fluid. Sheets typically have occlusive backing & adhesive perimeter to attach to peri-wound skin.	Good for autolytic debridement, granulation, and epithelialization in low to moderately exudative wounds. Hydrocolloid sheet with impermeable backing can be used to add occlusive cover over other dressings.	Caution in late repair phase, when adhesive perimeter may slow contraction. Caution if infection, since occlusive backing creates hypoxic environment that can favor anaerobes.
Hydrogel	Low Can add water back to wound.	90-95% water, comes as gel or as sheet that gels in wound. If lacks occlusive cover, add occlusive dressing on top to keep hydrogel's moisture in wound.	Dry wounds requiring autolytic debridement, granulation, or epithelialization. May enhance contraction on limb wounds.	May inhibit contraction on trunk wounds
Polyurethane film	Minimal Does not absorb or donate moisture.	Thin, flexible, transparent. Permeable to gas and water vapor, impermeable to water and bacteria. Adhesive perimeter adheres to peri-wound skin.	Wound with minimal exudate. Can use to provide semi-occlusive cover over other dressings. Especially good for epithelialization in a dry shallow wound or abrasion.	Don't use as primary dressing on wounds with more than minimal exudate.