HEALING BENEFITS FROM RESTORE



REFERENCES

- Theoret, Christine, and Jacintha M. Wilmink. "Exuberant granulation tissue." Equine wound management (2016): 369-384.
- Sen CK. "Wound healing essentials: let there be oxygen." Wound Repair Regen (2009): 17: 1.
- Lepault E, Céleste C, Dore M, et al. "Comparative study on microvascular occlusion and apoptosis in body and limb wounds in the horse." Wound Repair Regen (2005): 13: 520.
- 4. Falanga V, Zhou L, Yufit T. "Low oxygen tension stimulates collagen synthesis and COLIA1 transcription through the action of TGF-beta1." J Cell Physiol (2002): 191: 42.
- Dart AJ, Perkins NR, Dart CM, et al. "Effect of bandaging on second intention healing of wounds of the distal limb in horses." Aust Vet J (2009): 87: 215.
- Amedea B. Seabra, Joana C. Pieretti, Bianca de Melo Santana, Manuel Horue, Gonzalo R. Tortella, Guillermo R. Castro, "Pharmacological applications of nitric oxide-releasing biomaterials in human skin." International Journal of Pharmaceutics, (2023): 630: 122465.
- Furchgott, R. F., and Vanhoutte, P. M. "Endothelium-derived relaxing and contracting factors." FASEB J. (1989): 3: 2007– 2018.
- Kubes, P., Kanwar, S., Niu, X. F., and Gaboury, J. P. "Nitric oxide synthesis inhibition induces leukocyte adhesion via superoxide and mast cells." FASEB J (1993): 7: 1293–1299.
- Palmieri EM, McGinity C, Wink DA, McVicar DW. "Nitric Oxide in Macrophage Immunometabolism: Hiding in Plain Sight. Metabolites." (2020): 10(11):429.
- Han G, Nguyen LN, Macherla C, Chi Y, Friedman JM, Nosanchuk JD, Martinez LR. "Nitric oxide-releasing nanoparticles accelerate wound healing by promoting fibroblast migration and collagen deposition." Am J Pathol. (2012): 180(4):1465-73.

RESTORE LINE OF WOUND CARE PRODUCTS

Restore Wound Pads

Restore Wound Pads deliver potent nitric oxide technology for fast wound healing and are ideal for all wounds, especially exudative wounds.



5 x 7 cm Wound Pads 5 pads / box - \$99



5 x 12 cm Wound Pads 5 pads / box - \$149

- Designed for use over multiple days (2 7) resulting in less frequent dressing changes
- Provides a moist environment, ideal for wound healing
- Hydrocolloid components aid in exudate management
- Conforms to contours of the wound bed
- Used with veterinarian's choice of secondary dressings
- · Can be used in combination with other wound therapies
- Available in multiple sizes

Restore Wound Gels

Restore Wound Gel delivers faster healing with the same potent nitric oxide technology in hydrogel form which can be applied directly to the wound bed. Restore Wound Gel is ideal for large wounds, cavity wounds, complex geometries, or those in high motion areas.



5 mL Wound Gel 5 syringes / pkg - \$99

Available from these trusted sources:







This is not veterinary advice and Noxsano Animal Health recommends veterinarians refer to the product label and be trained in the use of this or any product before application.



© 2024 Noxsano Animal Health. All rights reserved. | www.noxsano.com | contact@noxsano.com | REV0224

RESTORE BY **BY NOXSANO**



THE PROMISING IMPACT OF NITRIC OXIDE ON PROUD FLESH

Convenient nitric oxide delivery for clinically proven accelerated healing and reduced proud flesh

Restore by Noxsano delivers nitric oxide to actively drive wound healing and mitigate infection for faster wound closure compared to current wound products.



smidwest
veterinary supply

quine wound management presents many problems for the practicing veterinarian. Wound contraction is often slow, increasing the risk of developing Exuberant Granulation Tissue (EGT) which slows or stalls healing and necessitates debridement. (1) Slow healing and chronic inflammation can also lead to weak and improperly perfused tissue and potentially scarring. Tensional forces on the wound can lead to wound expansion. Microbial contamination and biofilm growth are common and can prevent healing. Topical nitric oxide (NO), as delivered by Restore by Noxsano, offers a solution to these challenges.

PHYSIOLOGY OF EGT

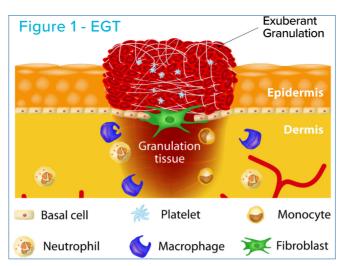
While EGT can be a thorn in the veterinarian's side, fibroplasia, the formation of granulation tissue, is a critical component of wound healing. Firstly, the granulation tissue fills in the gap left by the wounding event thus forming a barrier against environmental contamination. Further, the process produces myofibroblasts which exhibit a contractile force on the wound margins and creates a tissue bed over which epithelial cells migrate to complete wound closure.

From this tissue also comes endothelial cells, which form the vascular network of the newly grown tissue to bring oxygen and nutrients to the area. The vascular network also brings leukocytes into the area which attack and help clear contamination and debris from the wound.

Ideally, the wound transitions out of this granulation phase as the gap in the wound is filled, allowing healthy contraction and epithelialization to proceed. When this transition does not occur, EGT begins to grow (Figure 1).

Interestingly, low oxygen concentration has been shown to stimulate fibroblast proliferation and extracellular matrix formation. Oxygen is required for leukocytes to perform their antibacterial function efficiently. (2) Well perfused tissue is generally not hypoxic. Any veterinarian who has excised proud flesh has observed the significant bleeding that can occur due to extensive angiogenesis. While this might seem to be the sign of well perfused tissue, the lumen, or opening, of the newly growing vessels have been shown in EGT to be significantly more occluded than those in healthy wounds. (3) Hence, EGT is frequently more hypoxic than the heavy bleeding would seem to indicate.

Among the many causes of EGT, chronic inflammation stands out due to the frequency of occurrence in distal limb wounds and can be unrecognized because it often presents with a mild signature. Thus, strategies and treatments to mitigate chronic inflammation that are easy to apply and speed wound healing are also



highly desirable. In hypoxic environments, a prolonged response due to lack of oxygen may result in an extended period of inflammation. To further complicate the situation, hypoxia has been demonstrated to increase angiogenic and fibrogenic processes. (4)

TREATMENT, MITIGATION, AND PREVENTION OF EGT

Early stage wound management can dramatically affect the wound healing process and thus the propensity for developing EGT. Bandaging plays a critical role in successful distal limb wound healing but can result in an exacerbation of the conditions that results in EGT when done improperly. Even when done properly, multilayer bandaging with a primary dressing, an absorbent secondary layer to manage wound exudate, and a tertiary overwrap to support the other layers can still result in EGT formation, albeit with significantly less complications than poor bandaging techniques. (5)

When EGT does form, excision is often the most effective course of action. Removal of EGT allows the wound to transition from the fibroblastic phase of wound healing into the critical phases of contraction and epithelialization. It is advisable to be proactive and perform the procedure as soon as the granulation tissue protrudes above the wound bed while taking care to avoid damaging the migrating epithelium marching towards wound closure. Ideally, this will lead to wound closure without repeated excision, though the process may need to be repeated until wound closure proceeds normally. In most cases, when early treatment is utilized, this can be done with the horse standing and without the need for local anesthetics.

Beyond removing the excess, non-viable tissue, excision aids healing by removing any debris which may have entered the wound and rapidly reduces the leukocyte count in the superficial layer. This reduces stimuli present that incite chronic inflammation. When coupled with aseptic preparation of the surrounding skin, sterile bandaging, and utilizing topical antimicrobials to reduce bioburden, dramatic improvements in the health of the granulation bed are typically observed. Even the most skilled veterinarians utilizing the best procedures and conditions will find that this process may need to be repeated.

NITRIC OXIDE THERAPY VIA RESTORE

It is unlikely that a single silver bullet to prevent and resolve EGT will be discovered due to the wide range of underlying pathology. However, research in a number of contexts has demonstrated that topical delivery of nitric oxide can reduce wound healing times by regulating fibroblasts, inflammatory cells, cytokines, and remodeling proteins, improving the speed of closure and improving the strength and appearance of the regrown tissue. (10) All of these benefits (Figure 2) directly help with a significant reduction in EGT.

Nitric oxide occurs naturally in the healthy wound bed and topical application, as with Restore by Noxsano, in animals and humans has been studied over the past three decades. (6) Importantly, among its many roles in the wound healing process, NO has anti-inflammatory properties (7) and reduces leukocyte adhesion which drives the wound towards a healthy resolution. (8) It promotes angiogenesis and vasodilation resulting in well oxygenated tissue. The molecule is a naturally occurring antimicrobial and signals for macrophage polarization switch, a key step in the transition from inflammatory to postinflammatory stages of wound healing. (9)

Restore Wound Pads and Wound Gels are a powerful new tool for veterinarians to bring topical nitric oxide into their practice.

