
HAMBLETONIAN
PLACE

INNOVATIVE WOUND HEALING TECHNOLOGIES

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Classic Phases of Wound Healing

- Hemostasis
- Inflammation
- Proliferation
- Remodeling

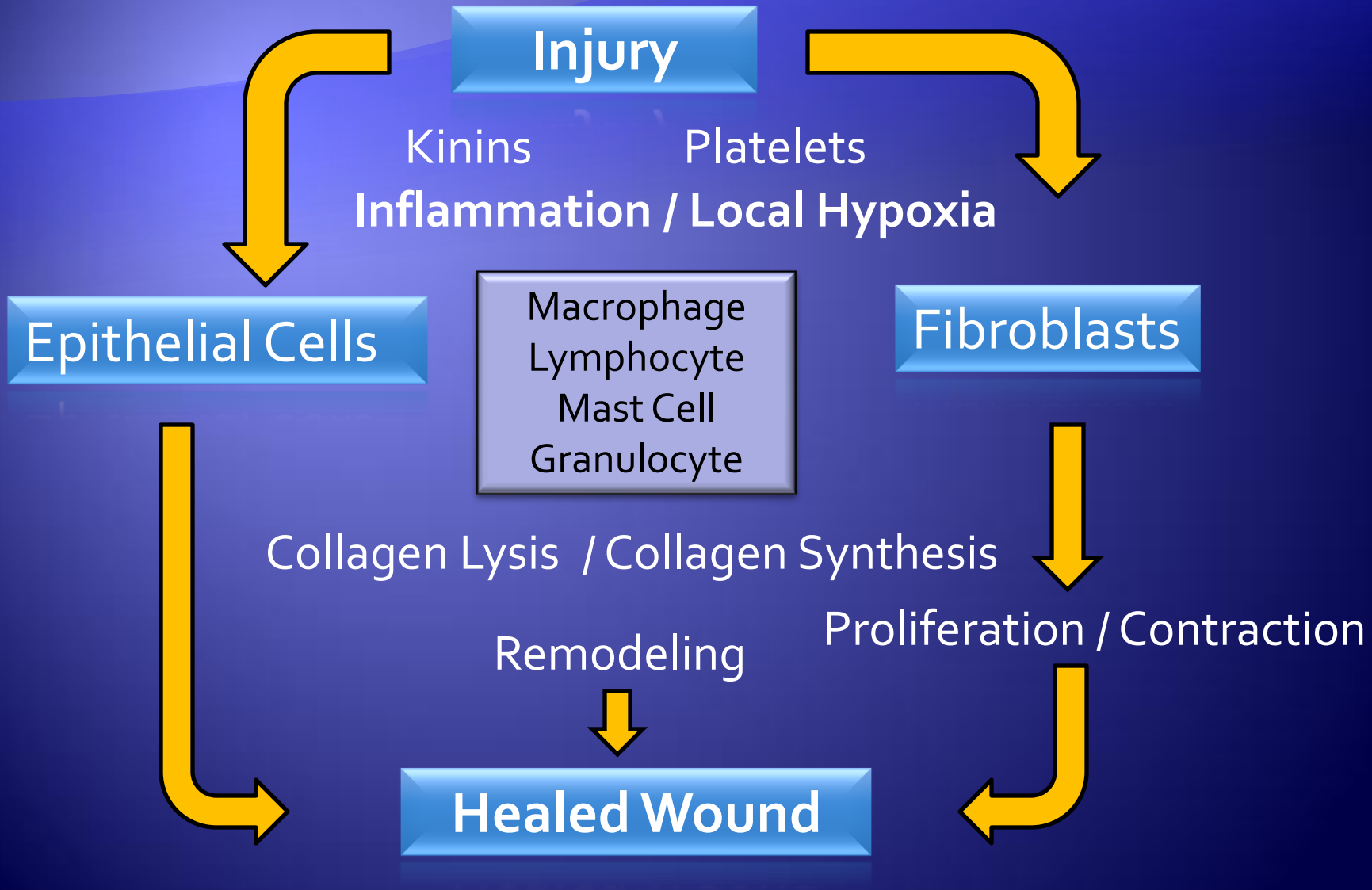
Mechanisms of Wound Healing

- Inflammation
- Matrix production
- Angiogenesis
- Epithelialization
- Remodeling

Factors that Impair Wound Healing

- Systemic factors
  - Age
  - Medical co-morbidities
- Local environmental factors
  - Bacterial load
  - Degree of inflammation
  - Oxygen tension
  - Vascular perfusion

Wound Healing Schematic



Strategies for Wound Treatment

- Support the processes that promote wound healing
- Eliminate processes that impair wound healing

Extracorporeal Shock Wave Therapy

- Expression of growth factors VEGF, TGF-B1 & IGF-1
- Reduces inflammation
- Dose-dependent

Extracorporeal Shock Wave Therapy

- R05 or R20 mm probe
- Energy flux density of 0.11 mJ/mm^2
- 500 Pulses , Q 7 days

Effects of extracorporeal shock wave therapy on wounds of the distal portion of the limbs in horses.

Morgan DD, et al. JAVMA 2009, 234(9)1154-1161

- Healing time for treated wounds (76 days) was significantly shorter than that of untreated wounds (90 days).
- ESWT may stimulate healing of wounds of the distal portion of the limbs in horses.
- Although the mechanism by which healing was stimulated could not be identified, extended expression of growth factors likely played a role.

Effects of unfocused extracorporeal shock wave therapy on healing of wounds of the distal portion of the forelimb in horses.

Silveira A, et al. AJVR 2010, 71(2)229-2334

- Treatment with ESWT did not accelerate healing of equine distal limb wounds, but treated wounds had less exuberant granulation tissue and appeared healthier than controls.
- ESWT may be useful to prevent exuberant granulation tissue formation and chronic inflammation of such wounds, but further studies are necessary before recommending ESWT for clinical application.

Hyperbaric Oxygen Therapy

Hyperbaric Oxygen Therapy

- Provides metabolic substrate (Oxygen)
- Reduces inflammation (Vasoconstriction)
- Kills bacteria (increased killing capacity of neutrophils & potentiates aminoglycosides)
- Suppresses toxin synthesis
- Stimulates growth factors & up-regulates receptors
- Activates & mobilizes stem cells

Effect of Hyperbaric Oxygen on the Growth Factor Profile of Fibroblasts

Thomas S. Kang, et al. Arch Facial Plast Surg 6(1):31-35, 2004

After 7 days of exposure to HBO_2 at 2 ATM cell proliferation was enhanced compared with controls. Secretion of growth factors (BFGF & VEGF) was increased in response to HBO_2 exposure.

HBO_2 exposure at 2 ATM enhanced the growth of fibroblasts, directly effecting fibroblast production of autocrine growth factors as the result of changes in cell signaling pathways. *Oxygen dosage was critical.*

Stem cell mobilization by hyperbaric oxygen

Stephen R. Thom, et al. Am J Physiol Heart Circ Physiol. 290: H1378-1386, 2006

Exposure to HBO_2 mobilized stem/progenitor cells from the bone marrow by a nitric oxide-dependent mechanism. The population of stem cells in the peripheral circulation of humans doubled in response to a single exposure to 2 ATA for 2 hours.

Pre-treatment of wild mice with a NO synthase inhibitor prevented the HBO_2 induced elevation in stem cell factor and circulating stem cells.

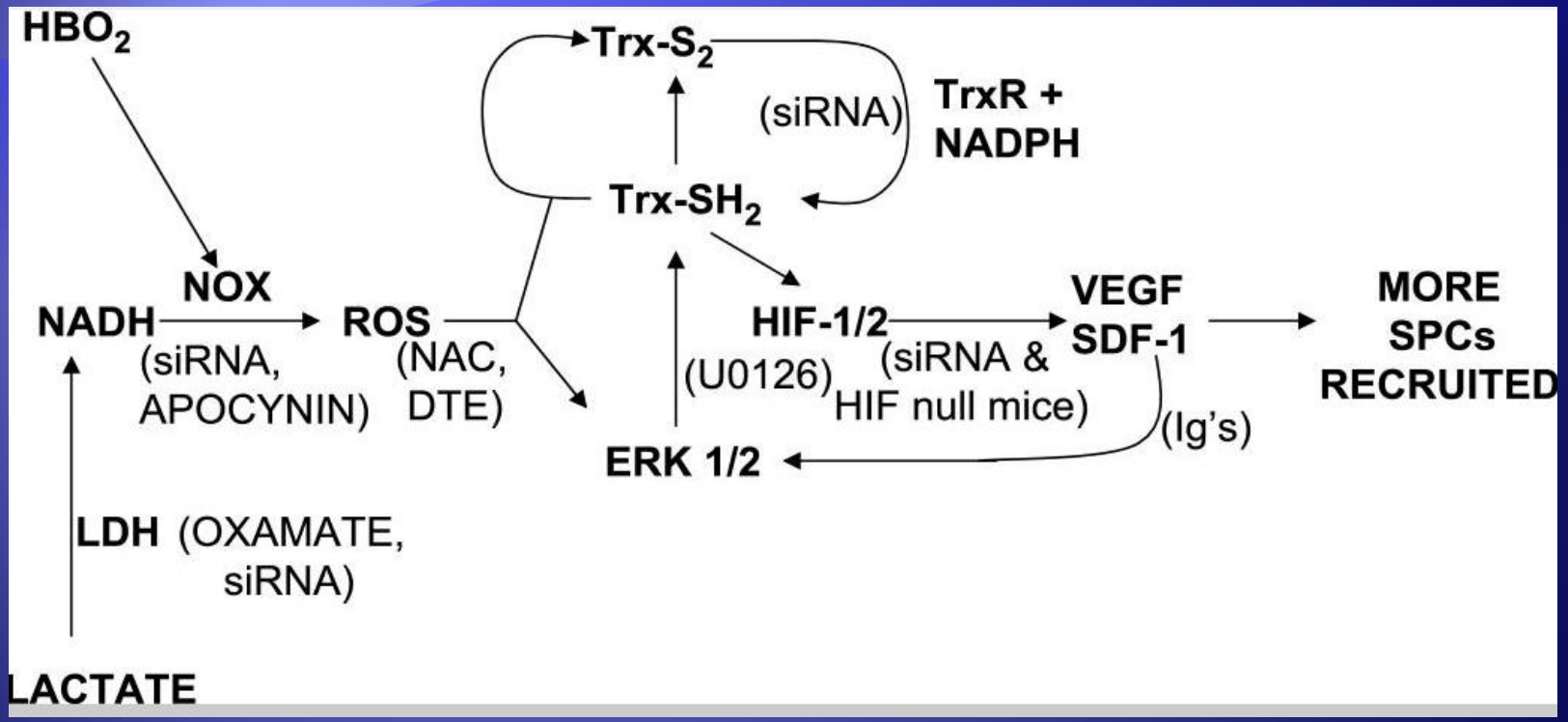
Hyperbaric oxygen stimulates vasculogenic stem cell growth and differentiation in vivo

Tatyana N. Milovanova, et al. J Appl Physiol. 2009 February; 106(2):711-728

Oxidative stress from HBO_2 (2.8 ATM) exerts a trophic effect on vasculogenic stem cells. In a mouse model, circulating stem/progenitor cell recruitment & differentiation were stimulated by HBO_2 and by a physiological oxidative stressor, lactate. In combination, HBO_2 and lactate had additive effects.

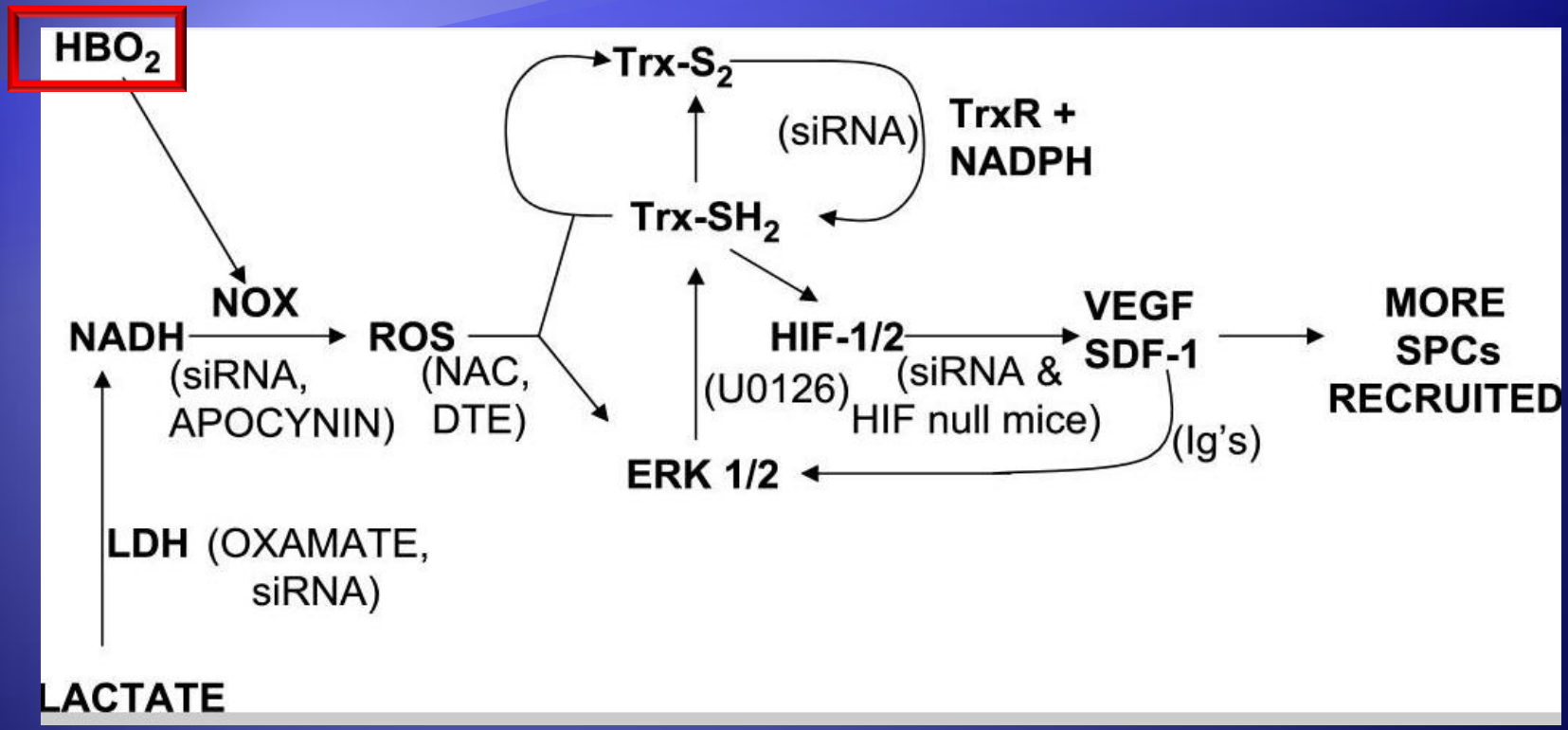
By causing an oxidative stress, HBO_2 activates a physiological redox-active autocrine loop in stem/progenitor cells that stimulates vasculogenesis by increasing the numbers of SPCs in blood and by increasing levels of cellular transcription factors.

Hyperbaric Oxygen Therapy



The "final common pathway" for SPC activation is stabilization and stimulation of HIF (hypoxic inducible factor) that turns on genes that make VEGF and SDF-1 which recruit SPCs. Tissue hypoxia is a constant natural stimulus through up-regulation of VEGF . HBO_2 creates increased reactive oxygen synthase, which in turn activates the thioredoxin loop which stabilizes HIF.

Hyperbaric Oxygen Therapy



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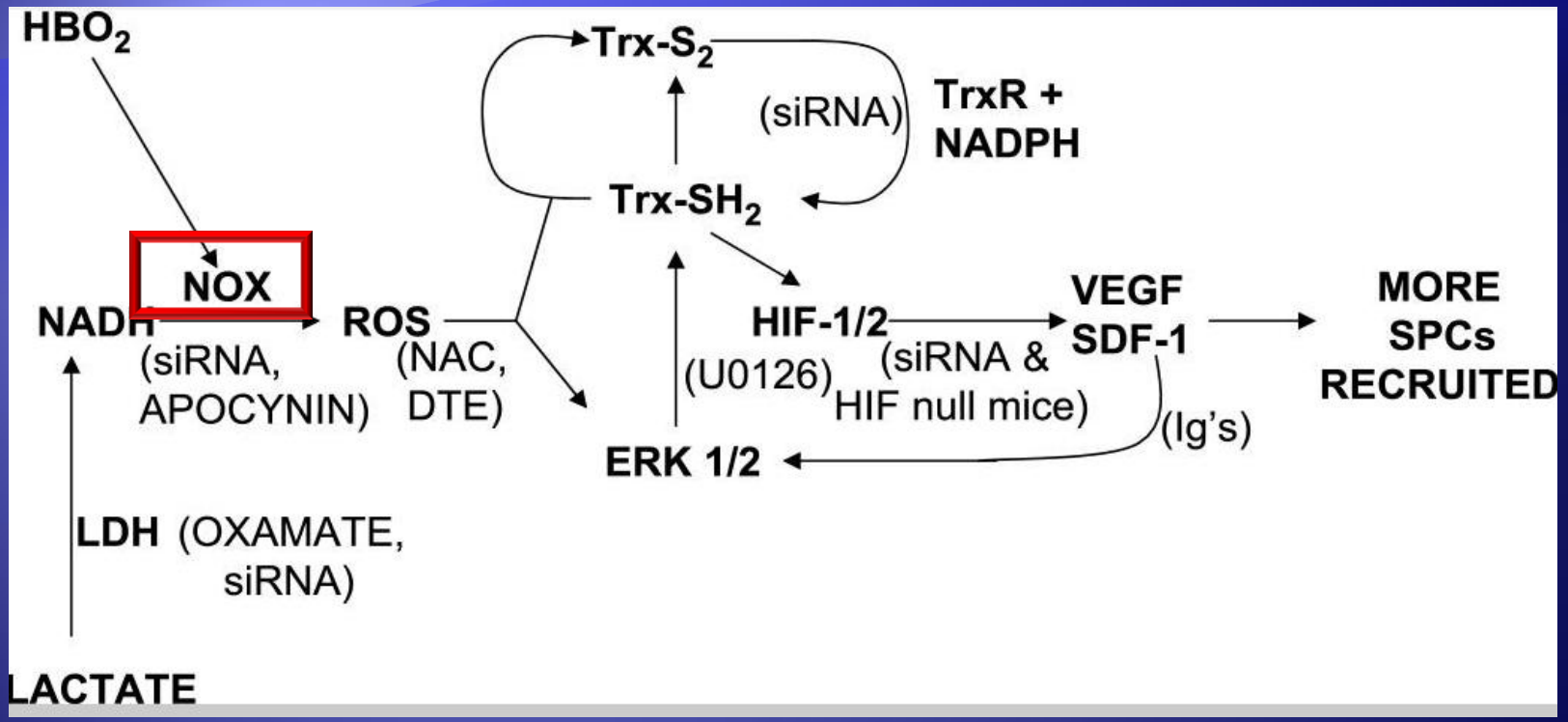

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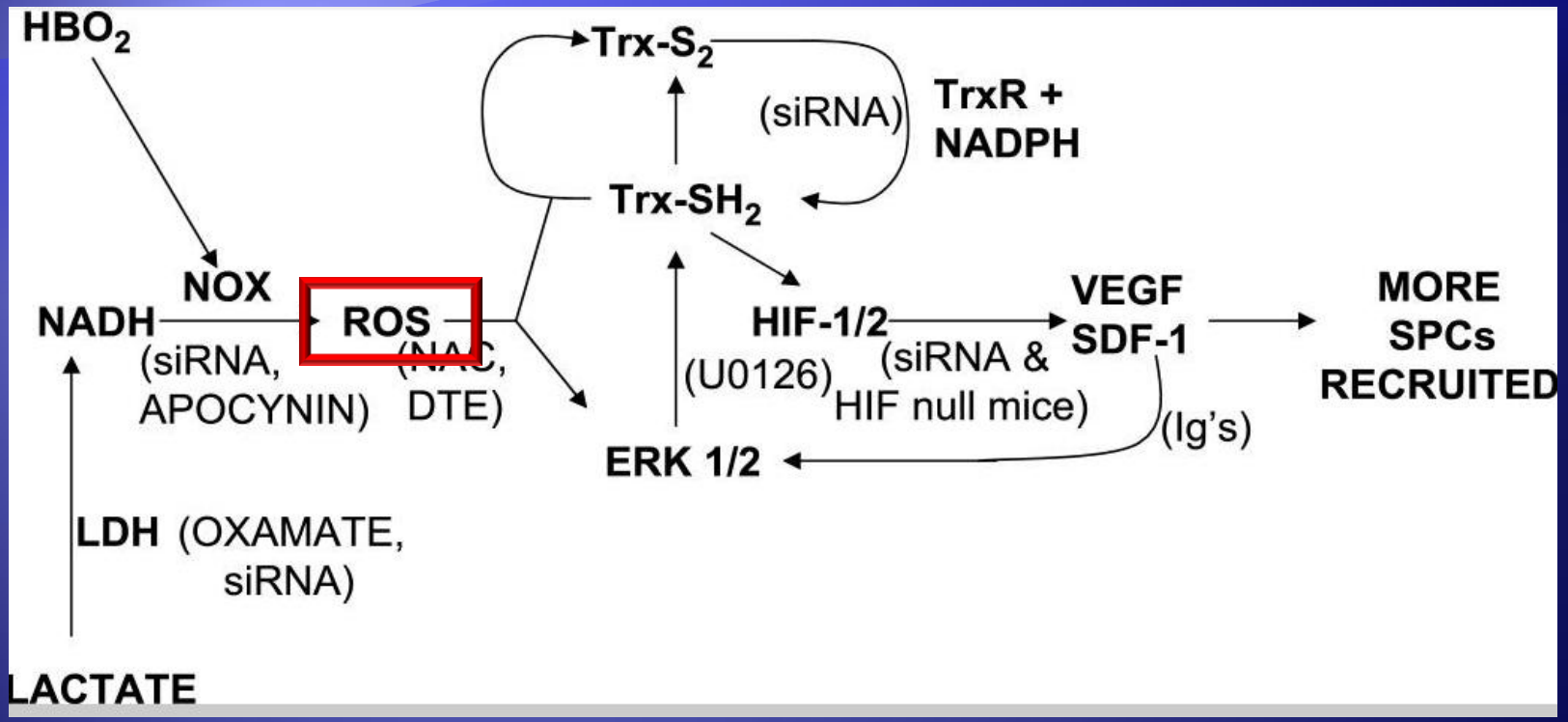

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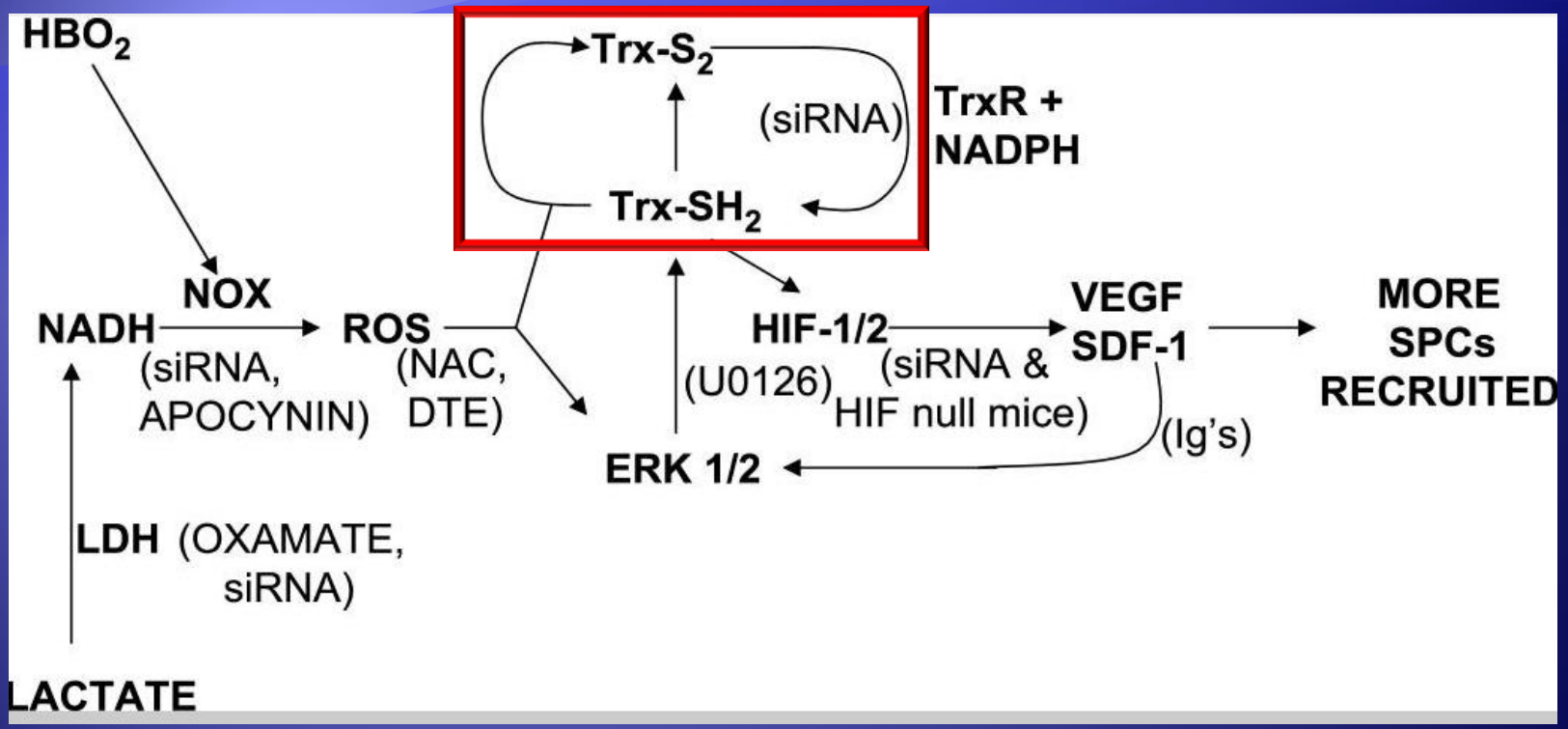

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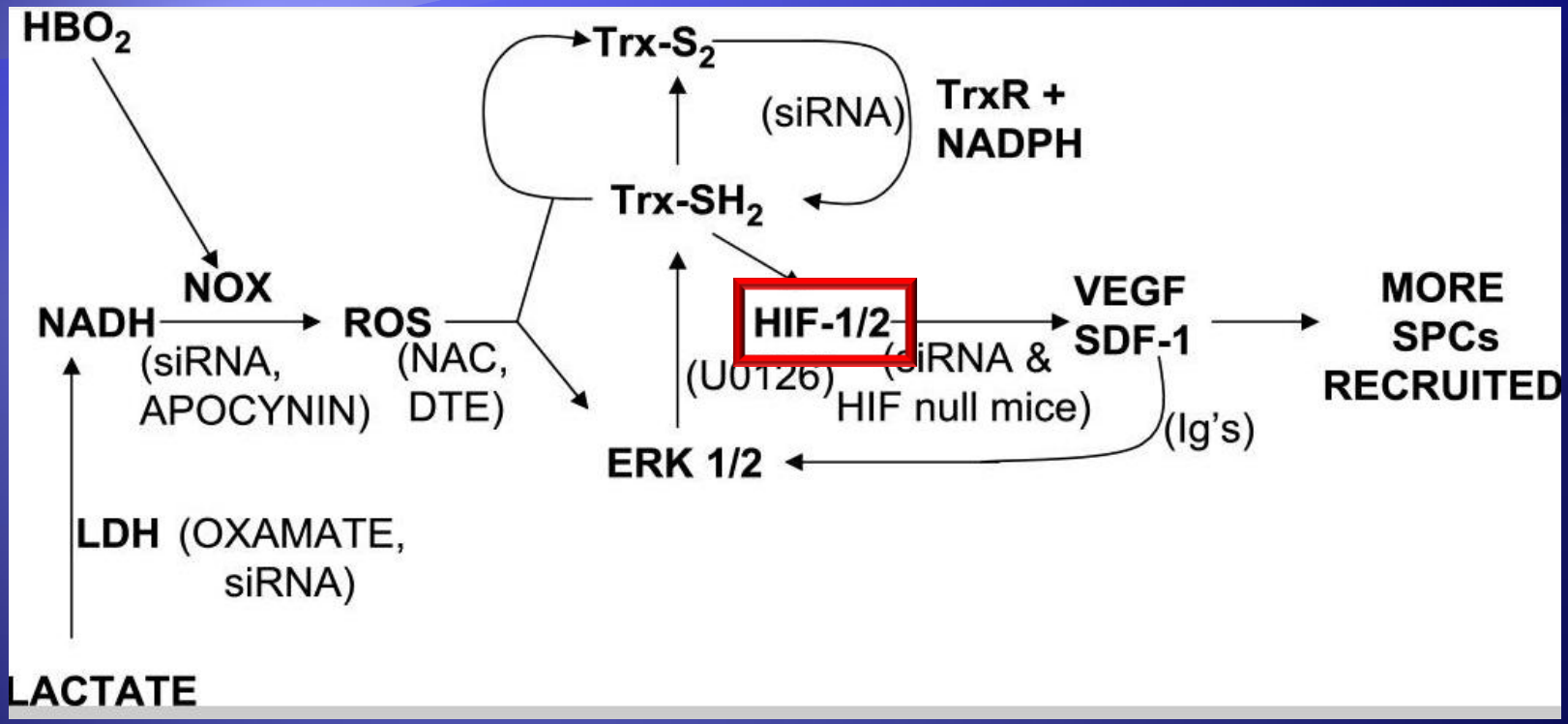

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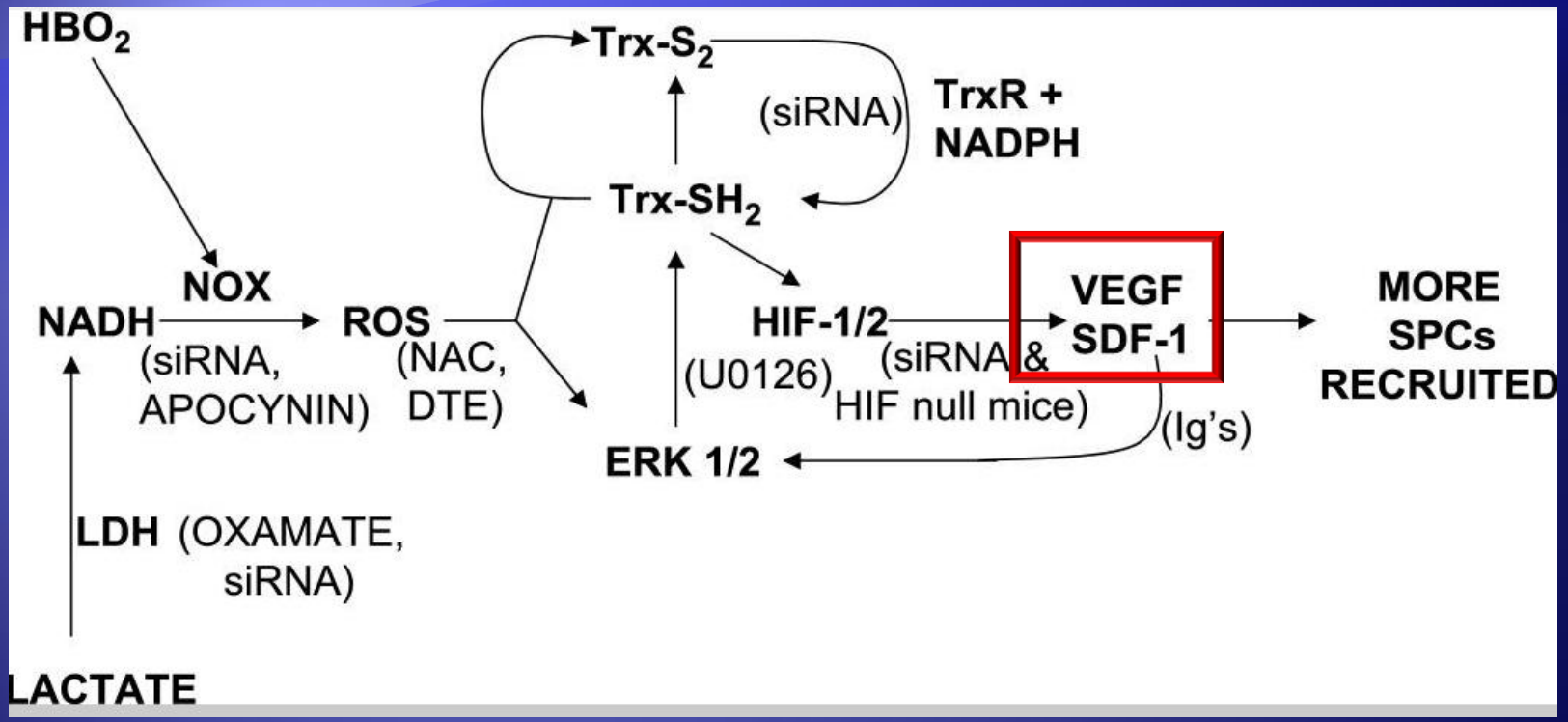

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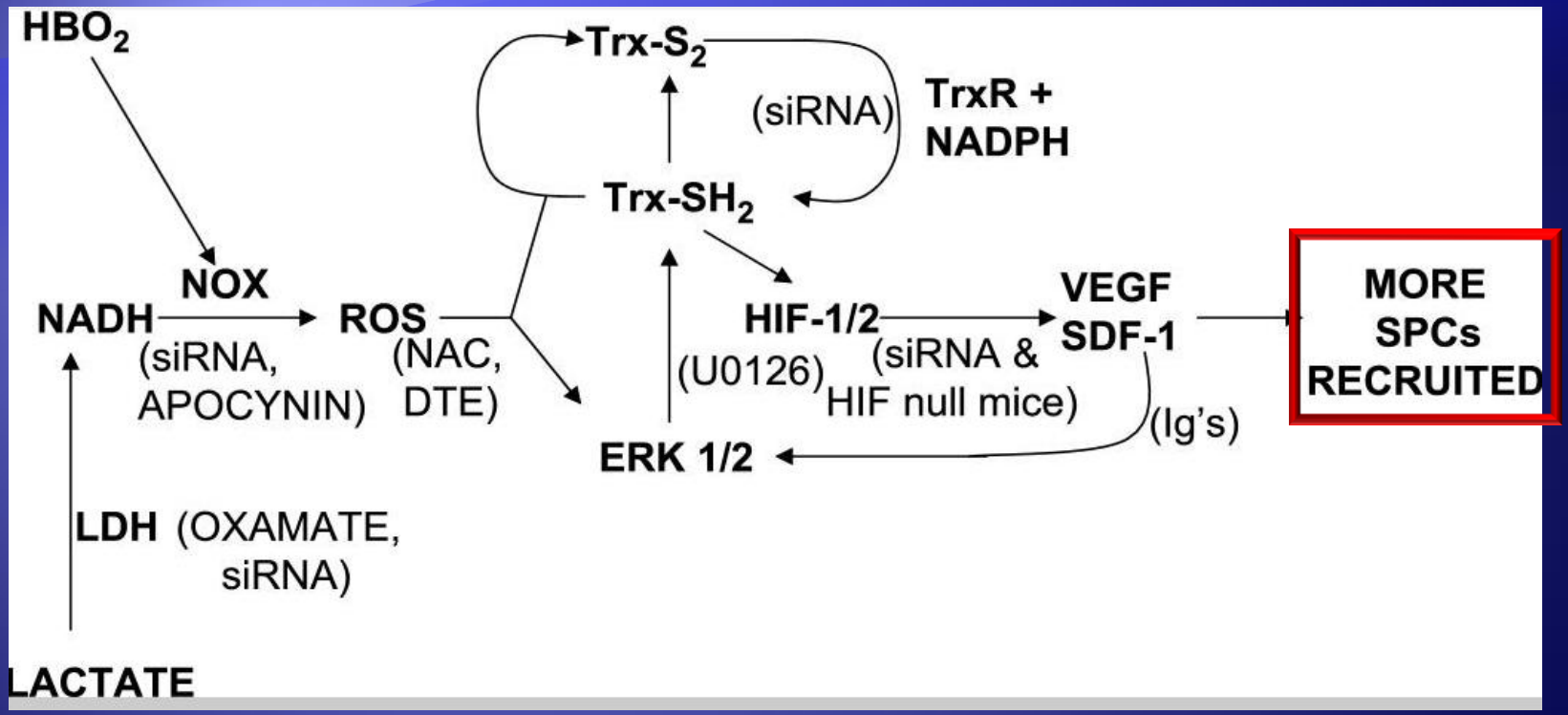

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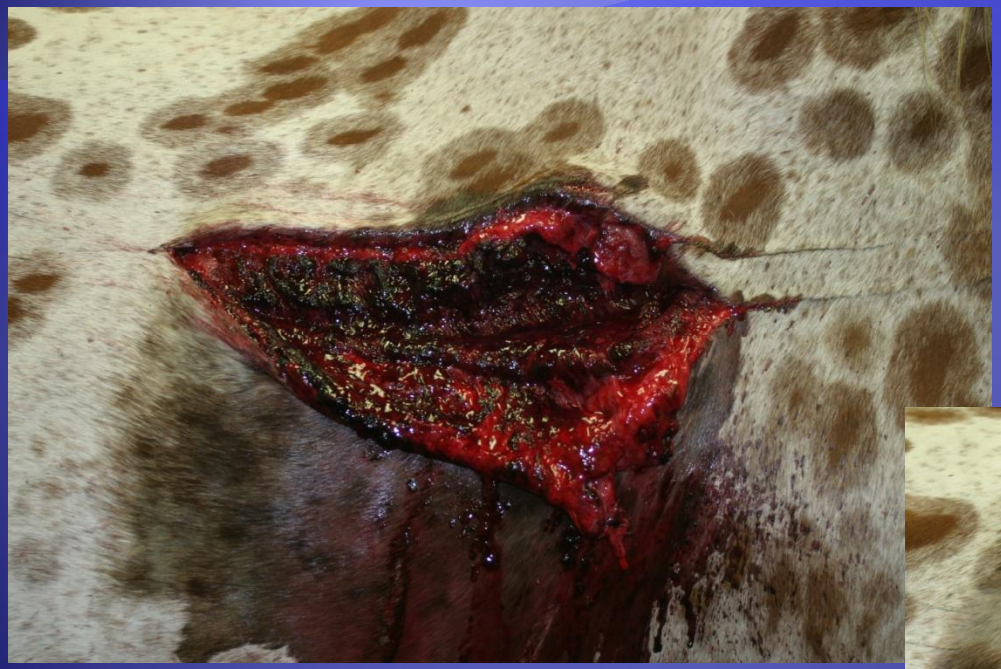


Hyperbaric Oxygen Therapy

PRP Therapy

- Provides concentrated growth factors by separating platelets & plasma from red & white blood cells
- Protective fibrin matrix may be injected into a wound or used as a wound dressing

Effects of platelet-rich plasma on the repair of wounds on the distal aspect of the forelimb in horses.

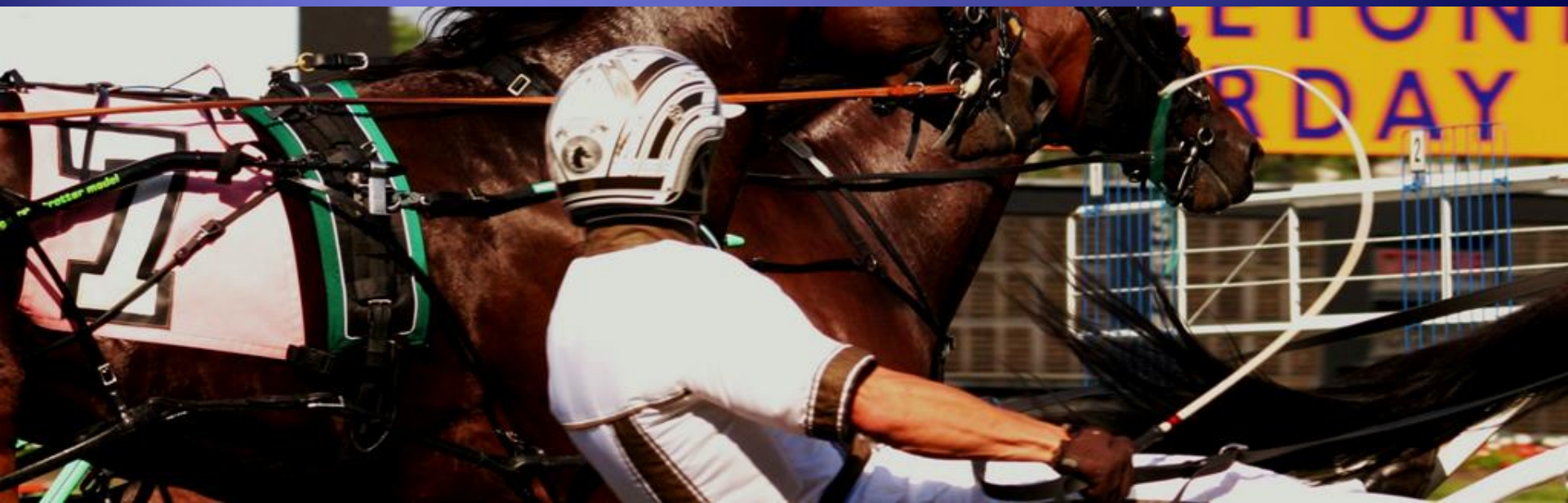
Monteiro SO, Lepage OM, Theoret CL. AJVR 2010 71(2)229-234

- Topical application of autologous platelet-rich plasma did not accelerate or improve the quality of repair of small granulating wounds on limbs of horses.
- This treatment may better suit wounds with massive tissue loss or, alternatively, chronic wounds that would benefit from a fresh source of mediators to accelerate the healing process.

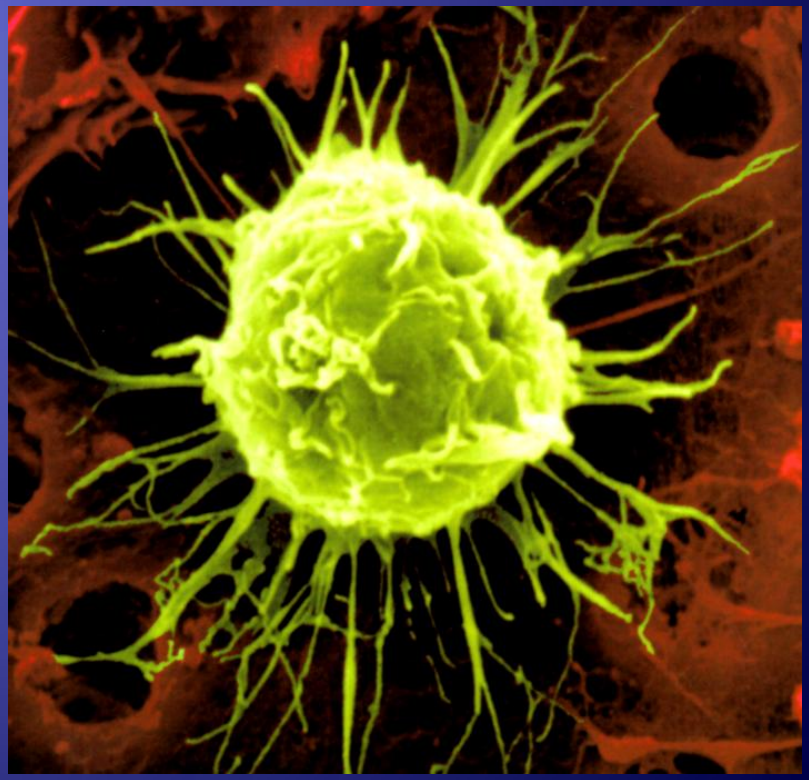
Bioactivity and stability of endogenous fibrogenic factors in platelet-rich fibrin

Lundquist R, Dziegiel MH, Agren MS. Wound Repair Regen 2008 16(3)356-363

- Platelet-rich fibrin provided sustained release and protection against proteolytic degradation of endogenous fibrogenic factors important for wound healing.

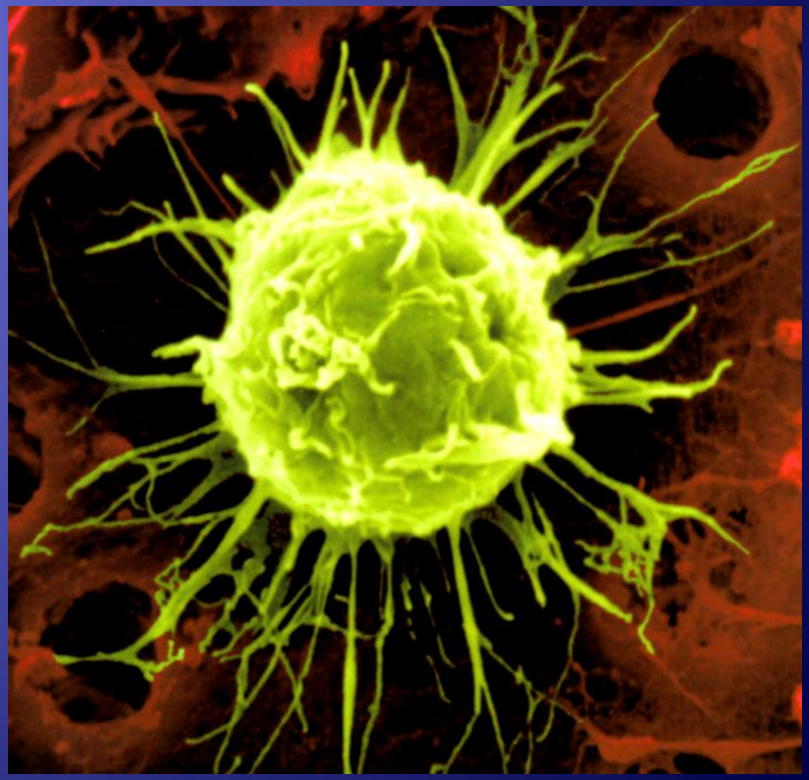


Stem Cell Therapy



Stem Cell Therapy

- Autologous Stem Cells
  - Same horse source
- Allogeneic Stem Cells
  - Other horse source



Stem Cell Therapy

- Mesenchymal Stem Cells
- Adipose Stem Cells
- Embryonic Stem Cells

Stem Cell Therapy

- Promotes proliferation of new blood vessels
- Stimulates growth factors
- Favors growth of normal tissue vs. scar tissue

Delivery of Stem Cells

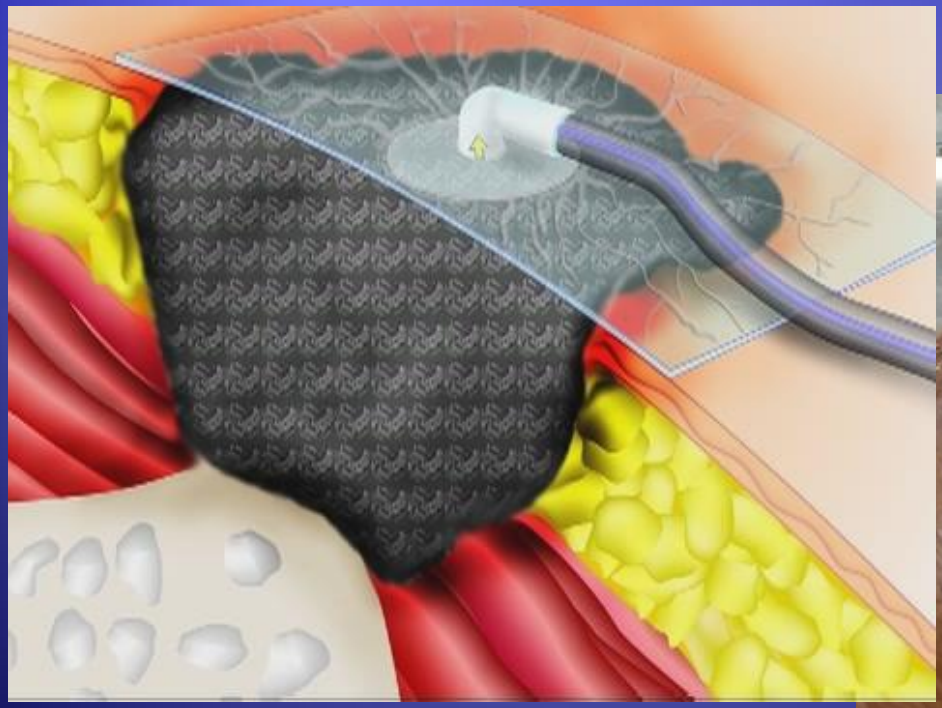
- Local infiltration
- Regional Limb Perfusion
- Intra-articular administration

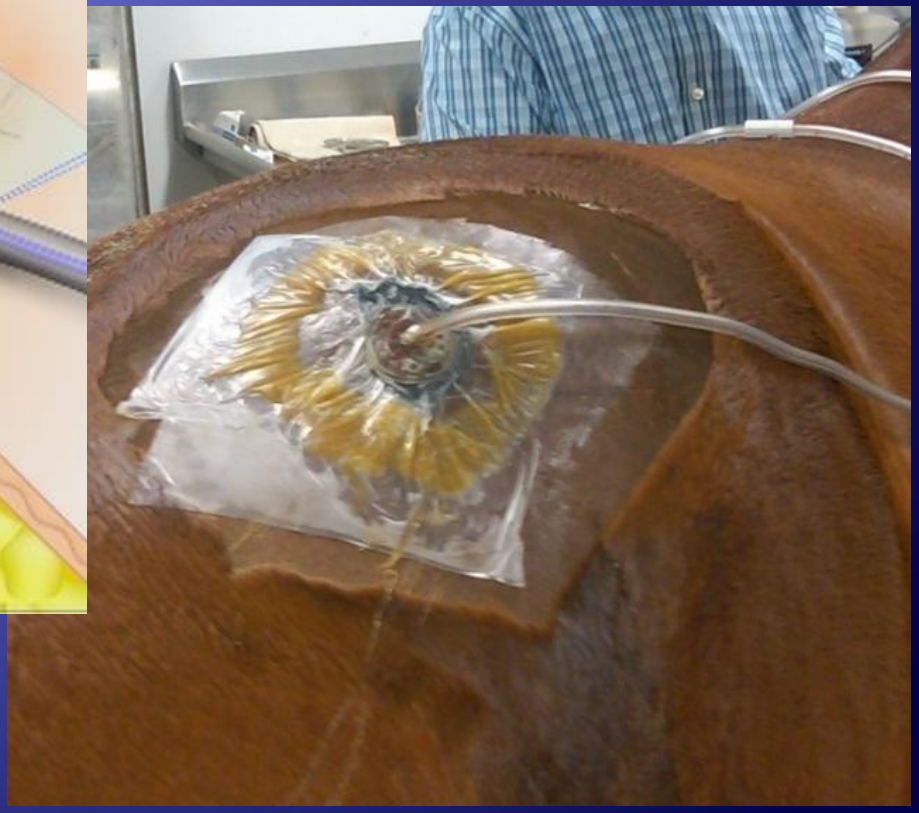
Regional Limb Perfusion

Spriet, M., North Am Vet Regen Med Conf, 2011

- Tourniquet placed above carpus for 45 min
- IA & IV administration of stem cells tagged with TcHMPAO
- 100% retention while tourniquet was in place
- Retention 6 Hours after administration:
  - IA - 39%, good diffusion in hoof & pastern
  - IV – 28%, 50% diffusion in hoof & pastern

Vacuum Assisted Closure (V.A.C.)® Therapy System



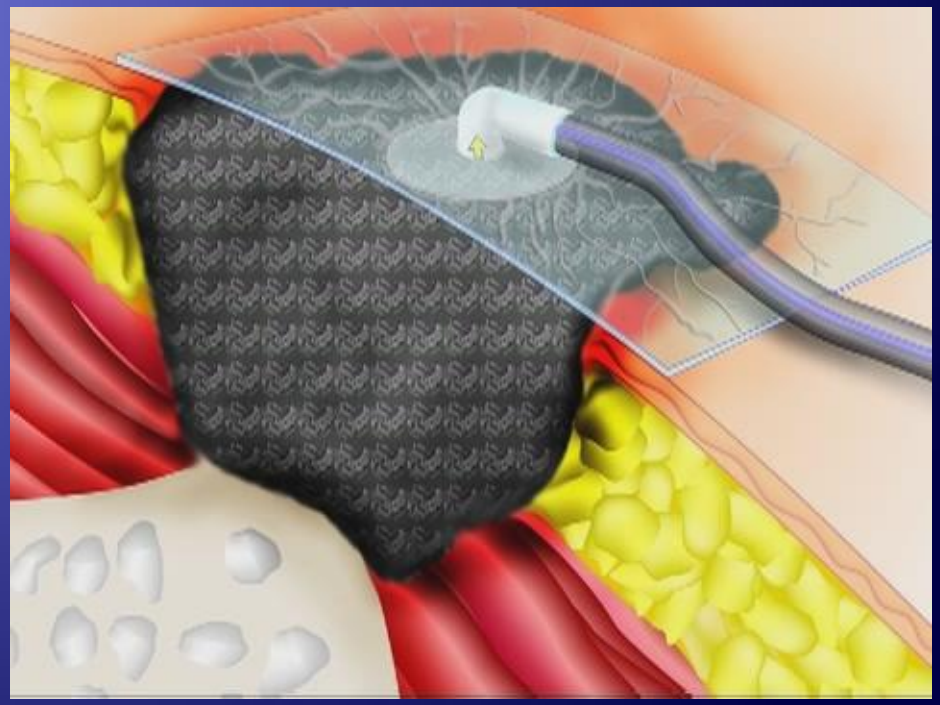


V.A.C.® Therapy System

- Widely used in human medicine.
- Creates sub-atmospheric pressure at the wound surface.
- Adjunctive therapy

  Used in conjunction

  with routine care.



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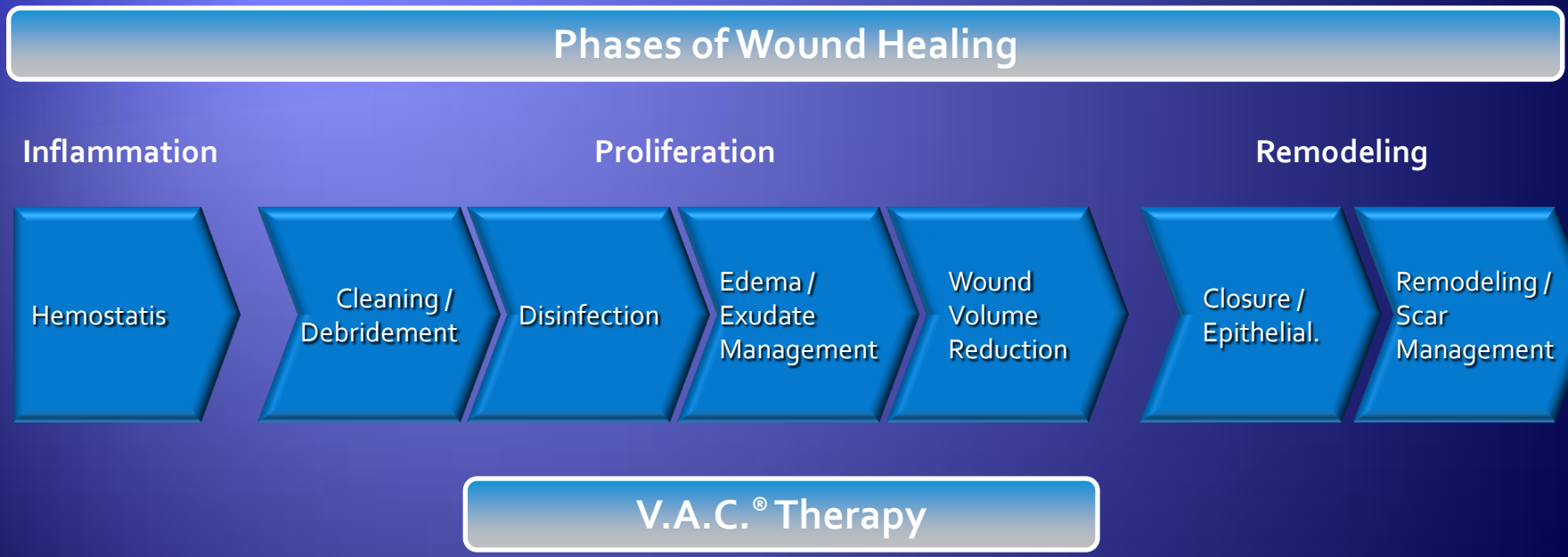

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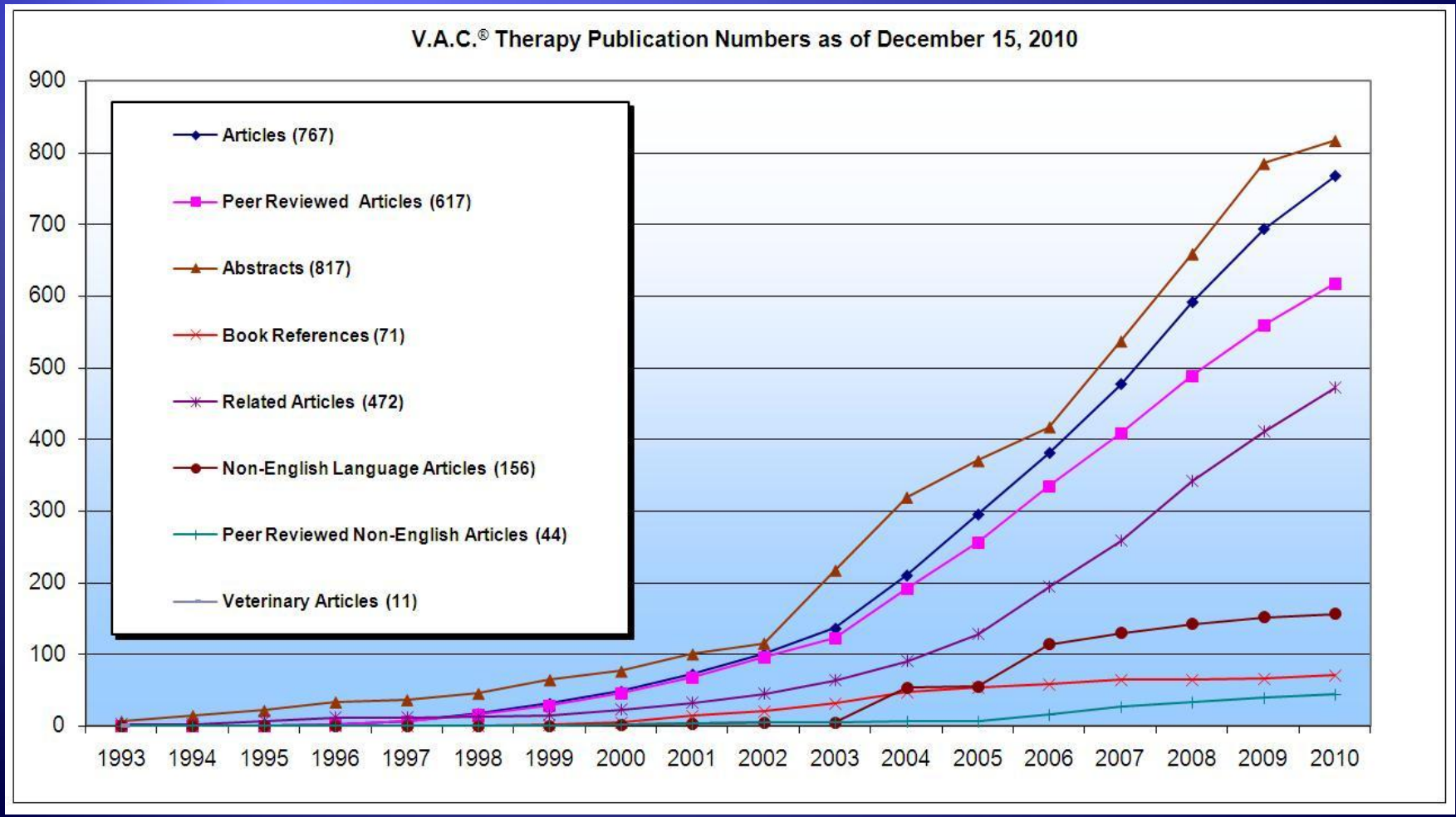
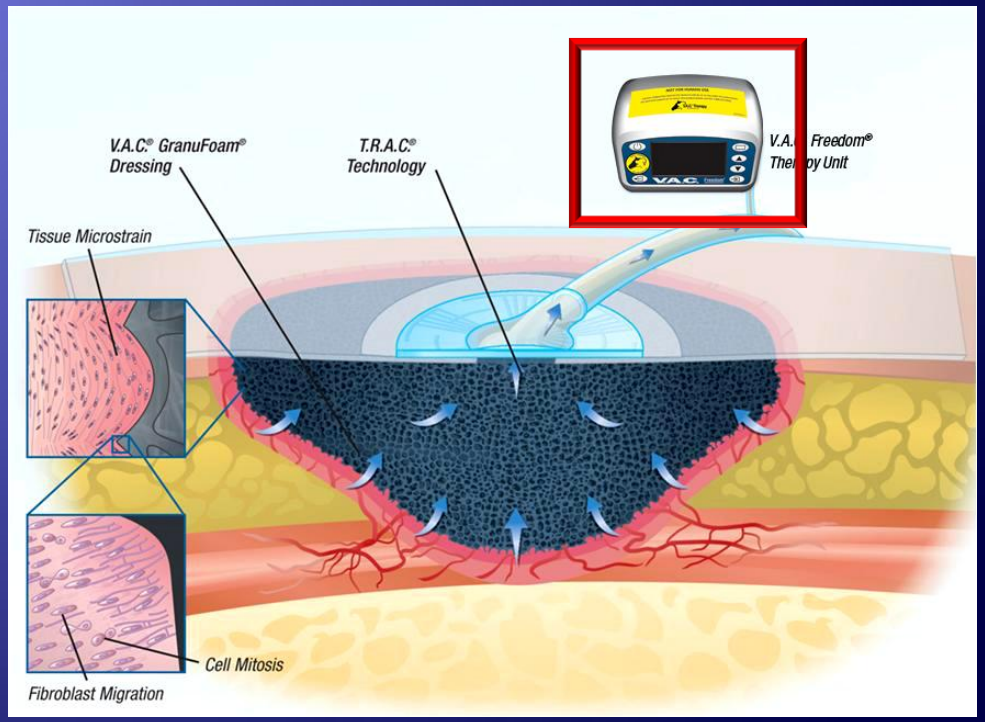


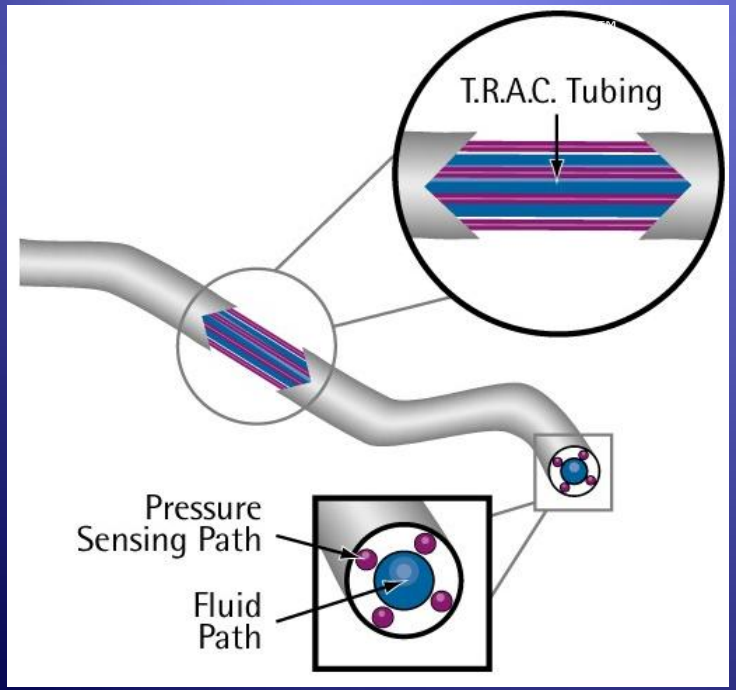
Components of V.A.C.®

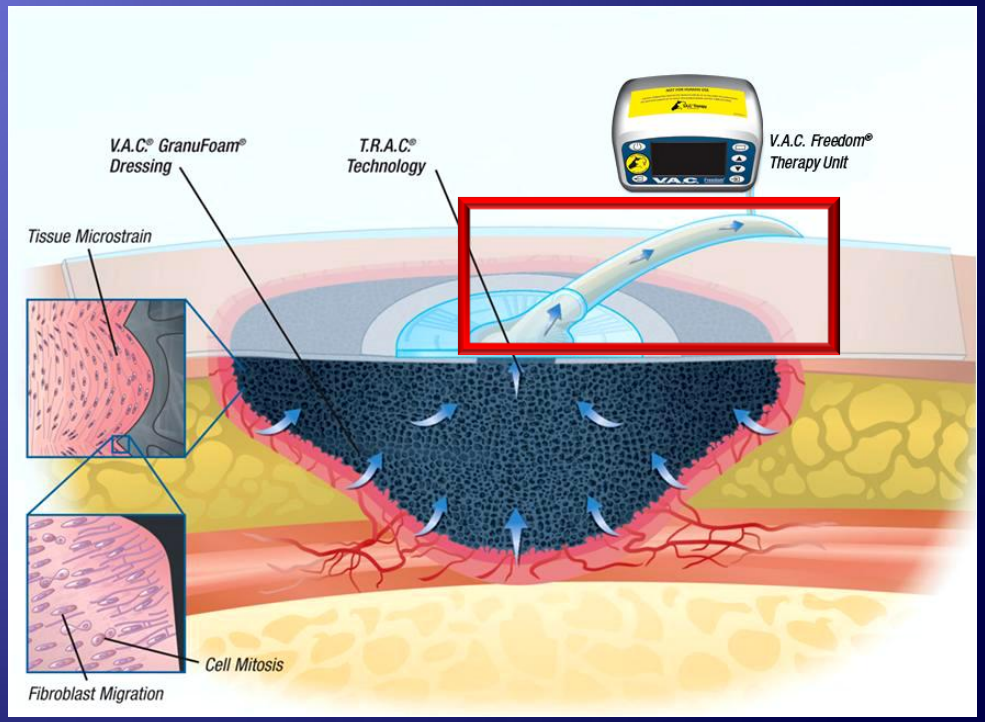
- Therapy Unit - provides intermittent/continuous sub-atmospheric pressure.



Components of V.A.C.®

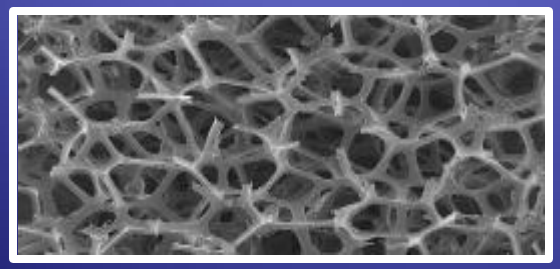
- Tubing & Canister - regulate pressure at wound site and collect exudate.

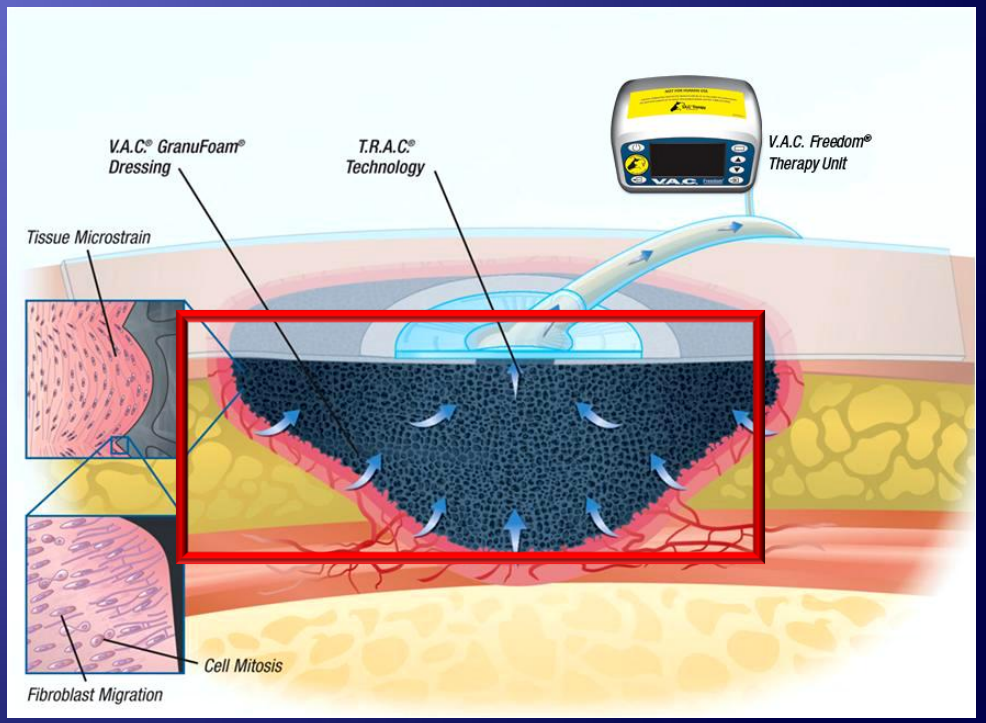




Components of V.A.C.®

- Hydrophobic polyurethane foam dressing - helps to promote granulation tissue formation / wound contraction.
- 400-600 micron pores

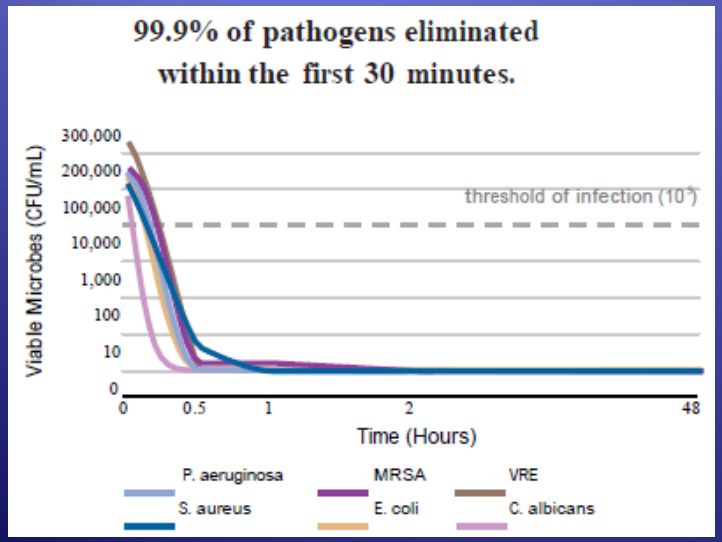


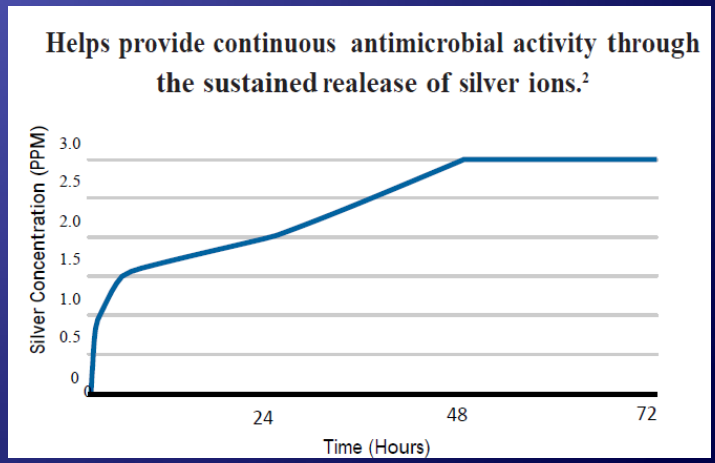


Granufoam® Silver Foam Dressing

- Combines antimicrobial effect of silver ions with sub-atmospheric pressure.

V.A.C.® GranuFoam® Silver™ Dressing provides direct and complete contact with the wound bed for continuous delivery of V.A.C.® Therapy and silver.

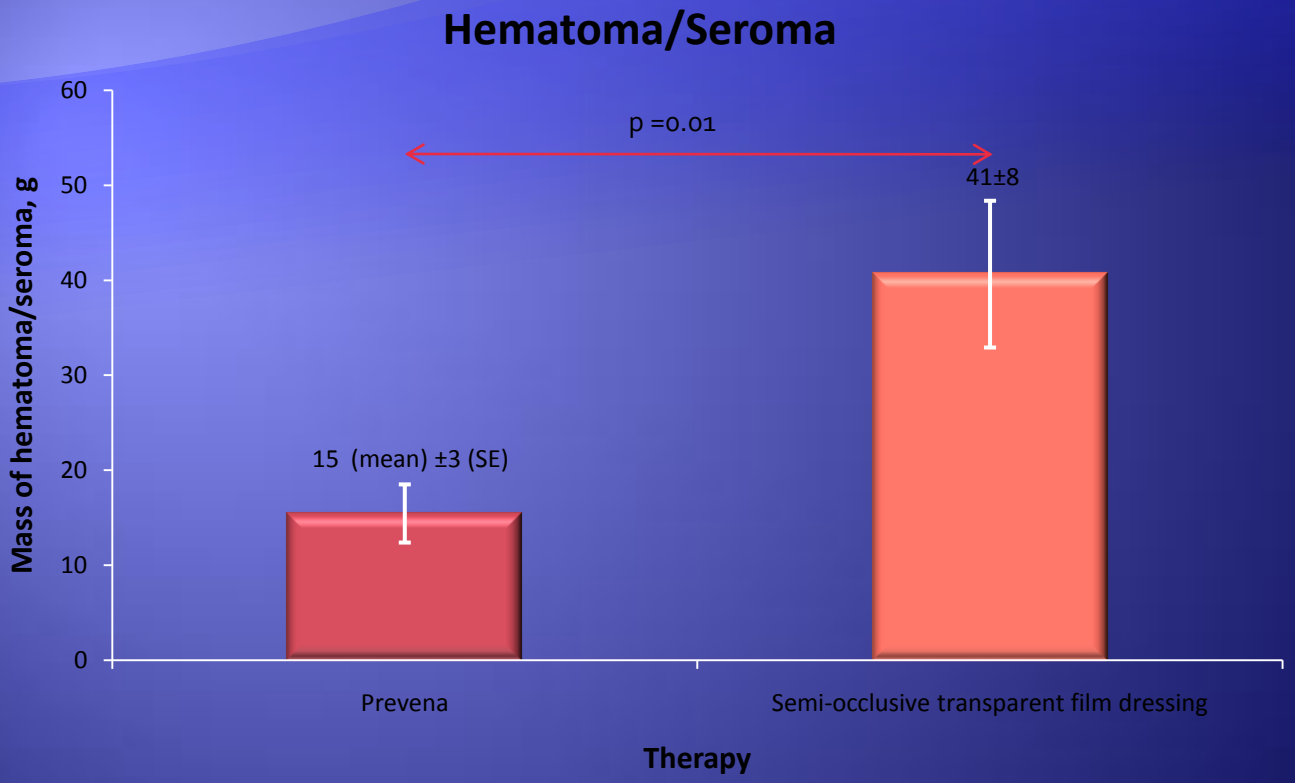




Sub-atmospheric pressure

- Promotes granulation tissue formation
- Reduces tissue edema & Promotes perfusion
- Removes exudate & infectious material

Sub-atmospheric pressure



- Porcine model hematoma/seroma formation was reduced after 4 days of negative pressure therapy (p=0.01)

V.A.C.®Indications

- Acute & chronic wounds
- Dehisced wounds
- Pressure ulcers
- Flaps / grafts
- Closed surgical incisions

V.A.C.® Treatment Protocol

- Remove hair adjacent to wound (5 to 10 cm margin)
- Thoroughly clean & debride wound
- Apply tag cement to adjacent skin
- Apply V.A.C. GranuFoam® dressing, drape & pad.

V.A.C.® Treatment Protocol

- Connect sensaT.R.A.C. tubing to therapy unit.
- Initiate V.A.C therapy at 125 – 200 PSI
- Monitor and treat for 48 hours
- Remove foam dressing and re-apply PRN

Case Example: Kick Wound Treatment Uutilizing V.A.C.® Therapy

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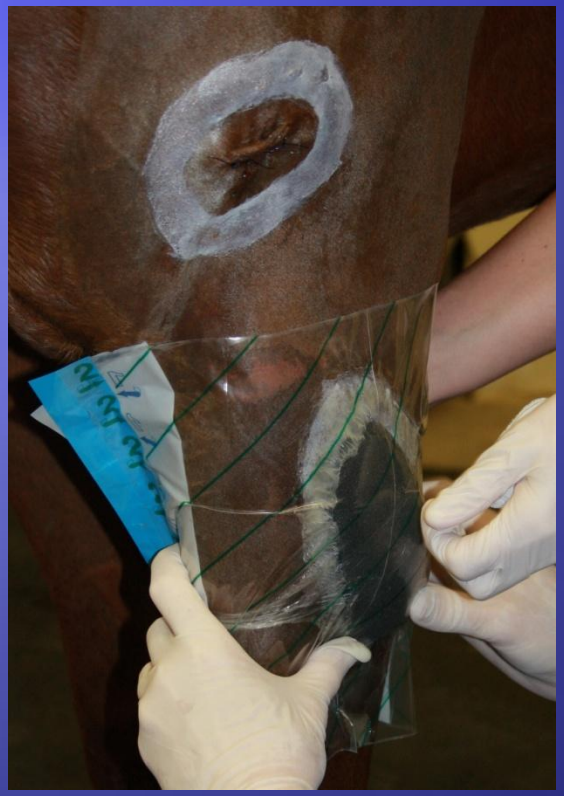
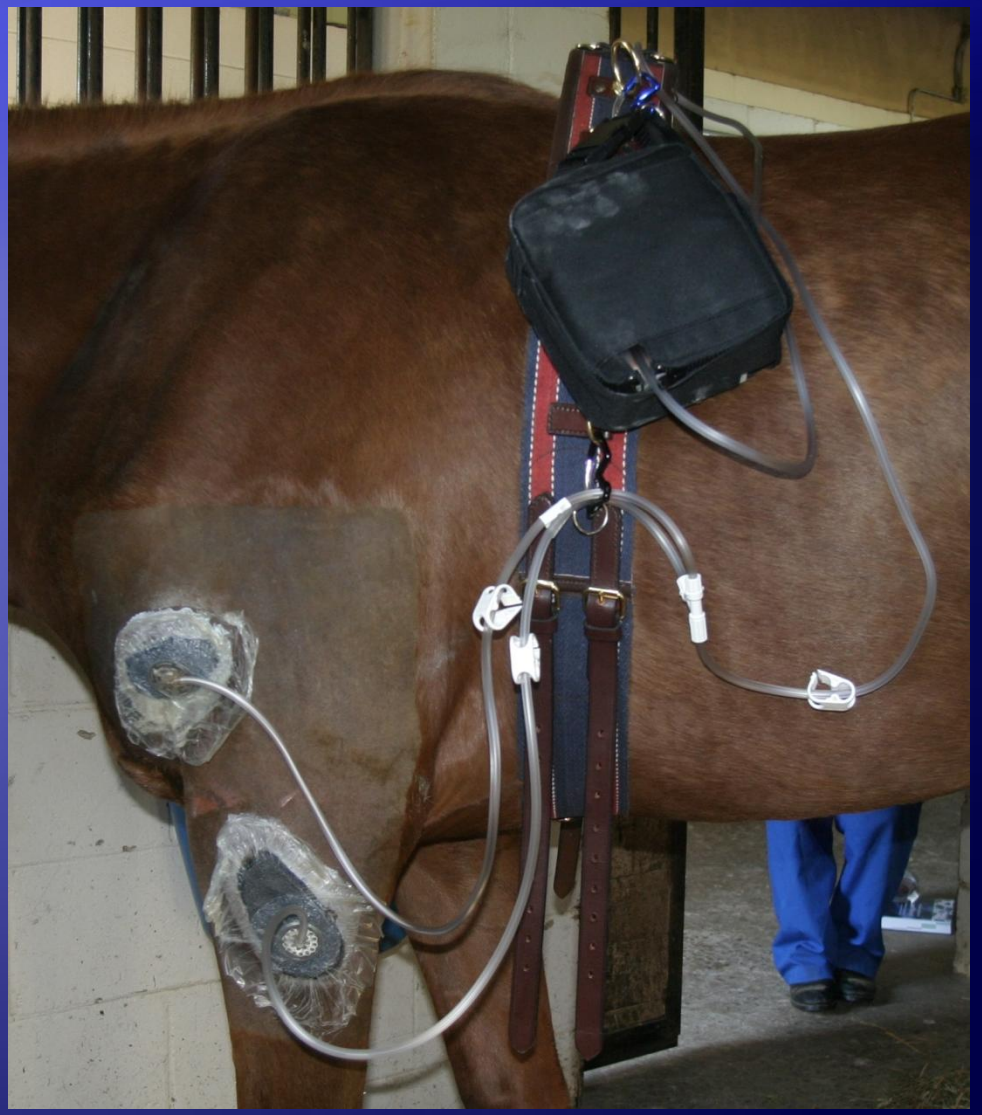


Case Example: Kick Wound Treatment Uutilizing V.A.C.® Therapy

- Effective adjunctive treatment for difficult wounds
- Logistical issues may be challenging



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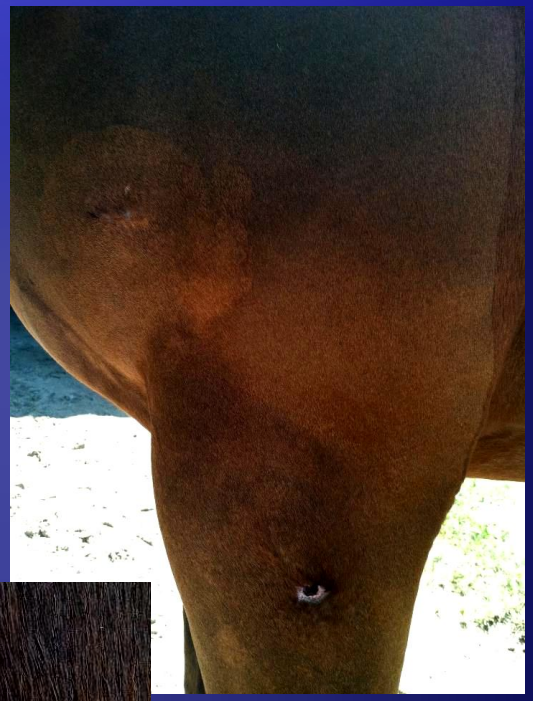


Case Example: Negative Pressure Therapy Used with a Closed Incision V.A.C.® Therapy

- Porcine Incision

  5 days Post-op - Control

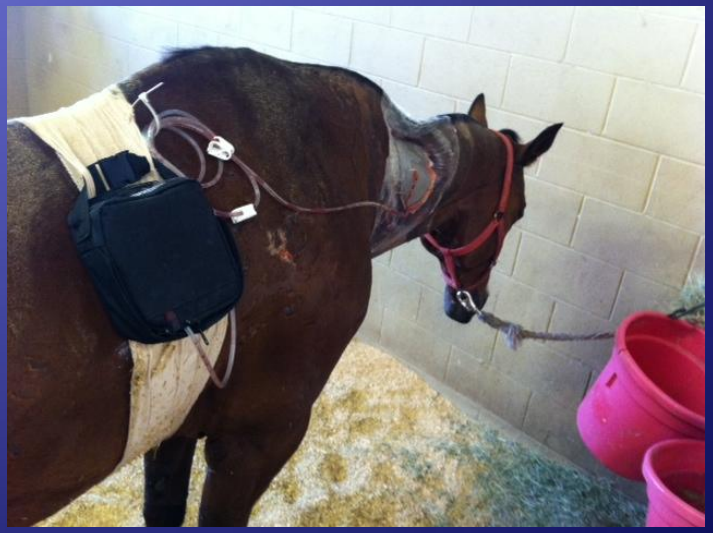
- Porcine Incision

  5 days Post-op – V.A.C. Therapy

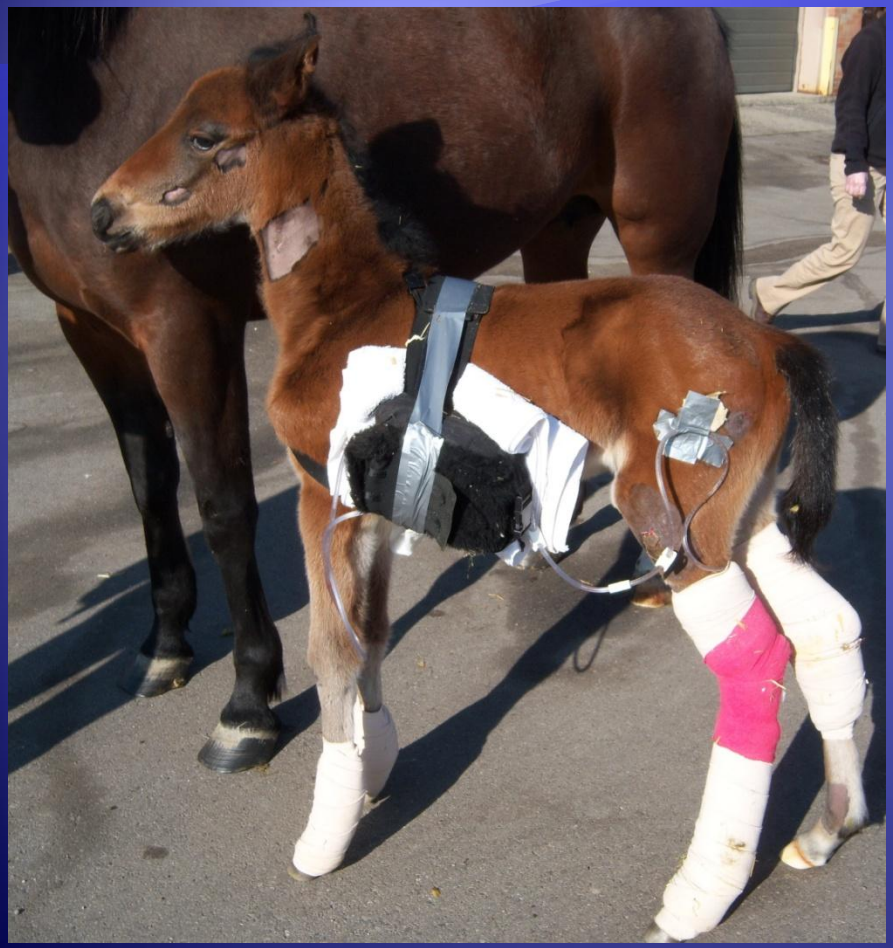
Incision tensile strength 6-10 times greater than control after 3 days of Negative Pressure Therapy

** Data courtesy of Dr. Yaszay, Children's Specialist Foundation*

Case Example: Mare neck injury treatment utilizing V.A.C.® Therapy – Courtesy Dr. Booth, KCI



Case Example: Foal with Frostbite
V.A.C.® Therapy - Courtesy Dr. Booth, KCI



Comprehensive Wound Therapy

- Hyperbaric Oxygen Therapy is often used in combination with stem cells & growth factor treatment.
- Hyperbaric Oxygen Therapy is also used in conjunction with V.A.C.® wound therapy.*

*V.A.C. Therapy Unit should not be taken into a HBOT chamber
Do not clamp tubing prior to HBOT treatment session.

Thank You & Enjoy the Hambletonian!