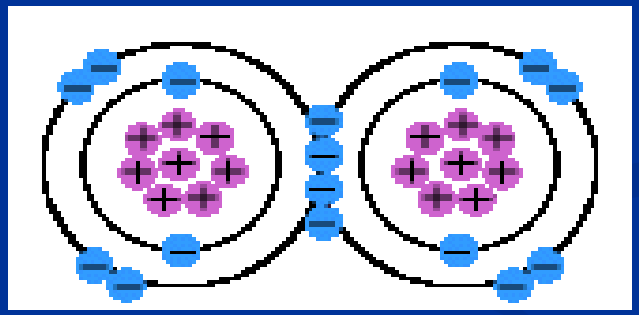
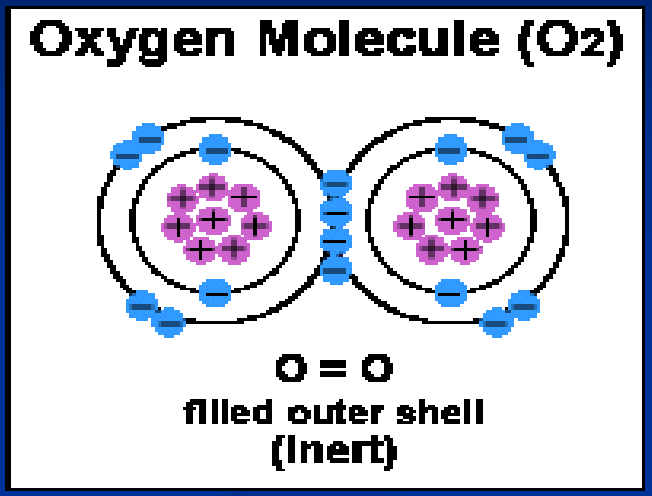
Supplemental Oxygen and Wound Healing

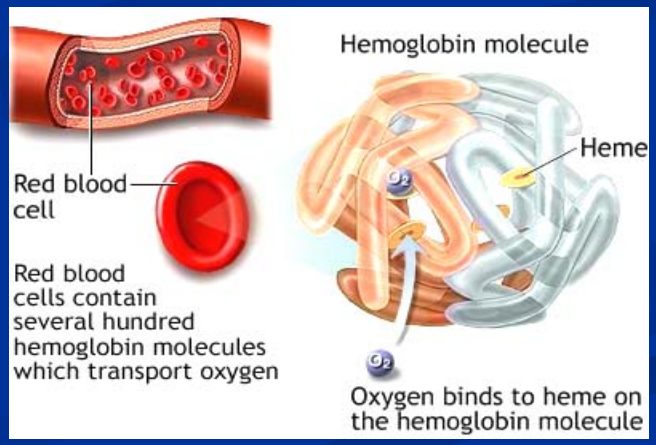


Bonnie Nicklas, DPM DABPS
Assistant Professor, Surgery CWRU
VA Pittsburgh Healthcare System

Oxygen and Wound Healing

Low oxygen concentration can arrest the process of wound healing.





LaVan, FB, Hunt, TK,. Clin Plast Surg. 1990

Objectives

- Historical review of O_2 and wound healing
- Physiology of O_2 and wound healing
- Current vehicles for delivery of O_2
- New technology for delivery of O_2
- Case Presentations

Historical Review

- 1600's-present: Hyperbaric technology
- 1775: Joseph Priestly discovers oxygen
- 1960's: Topical O2 to improve healing (THO)
- 1970's: HBO Com def 4 categories of clinical usage
- 2003: Transcutaneous injection: ligament healing
- 2004: Transcutaneous topical application: intermit
- 2005: Transdermal sustained continuous O2 therapy
- 2007: Topical oxygen emulsion

Physiology

Oxygen:

- Nutrient
- Antibiotic
- Drives redox-sensitive gene expression

Wound Repair Regen. 2003 Free Radic Biol Med 2008 Mol. Ther. 2006

Oxygen and Wound Healing

Physiology

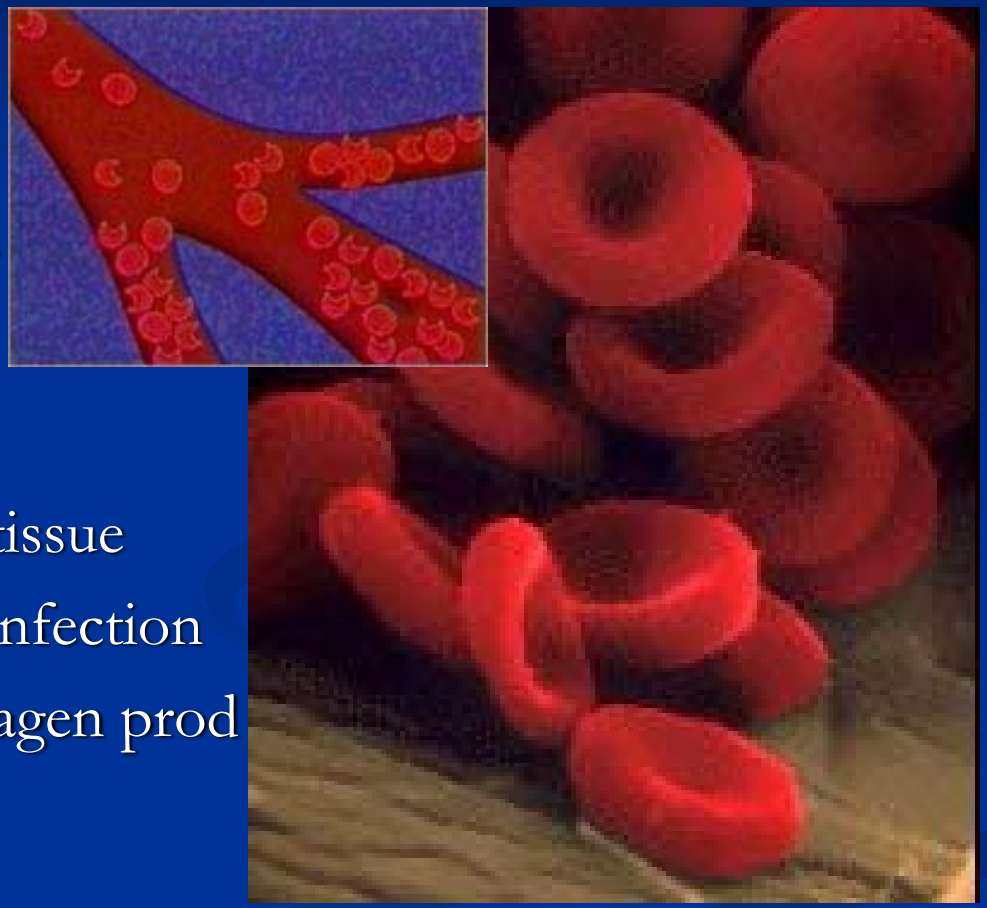
At cellular level Oxygen is metabolized

- Stimulates increase in growth factors
- Stimulates epithelialization
- Granulation tissue formation
- Glycosaminoglycan production
- Collagen synthesis
- NO: antibiotic effect

Am J. Surg 2003 N Eng. J. Med 2000 World J. Surg 2004

Oxygen and Wound Healing

- Wounds do not heal in tissue that does not bleed.



- Blood carries Oxygen.
- O_2: helps produce granulation tissue
  ensures resistance against infection
  effects fibroblasts and collagen prod

World J Surg. 2004 Oct;28(10):1068-9; Dennis Kunkle, Univ of Hawaii

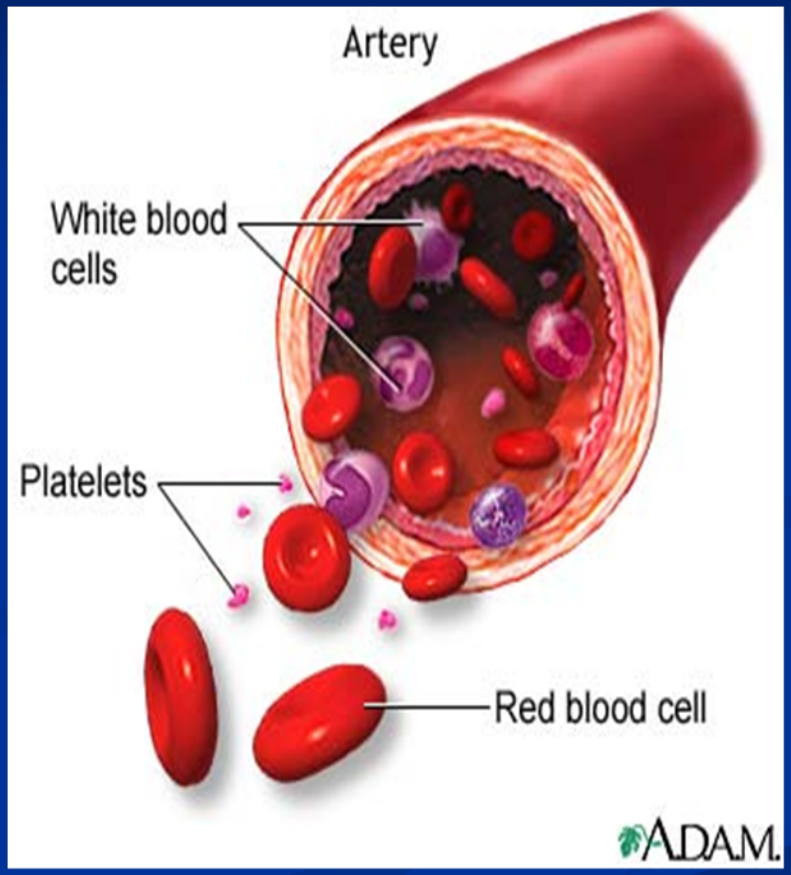
Blood: Essential for Wound Healing

- Blood supply: Vessels & Cells
  Blood: only fluid tissue in the body.

- Transportation:
  Delivers O2 and nutrients
  Returns waste and CO2.

- Distribution: nearly everything

- Protection: clot formation
  prevention of infection



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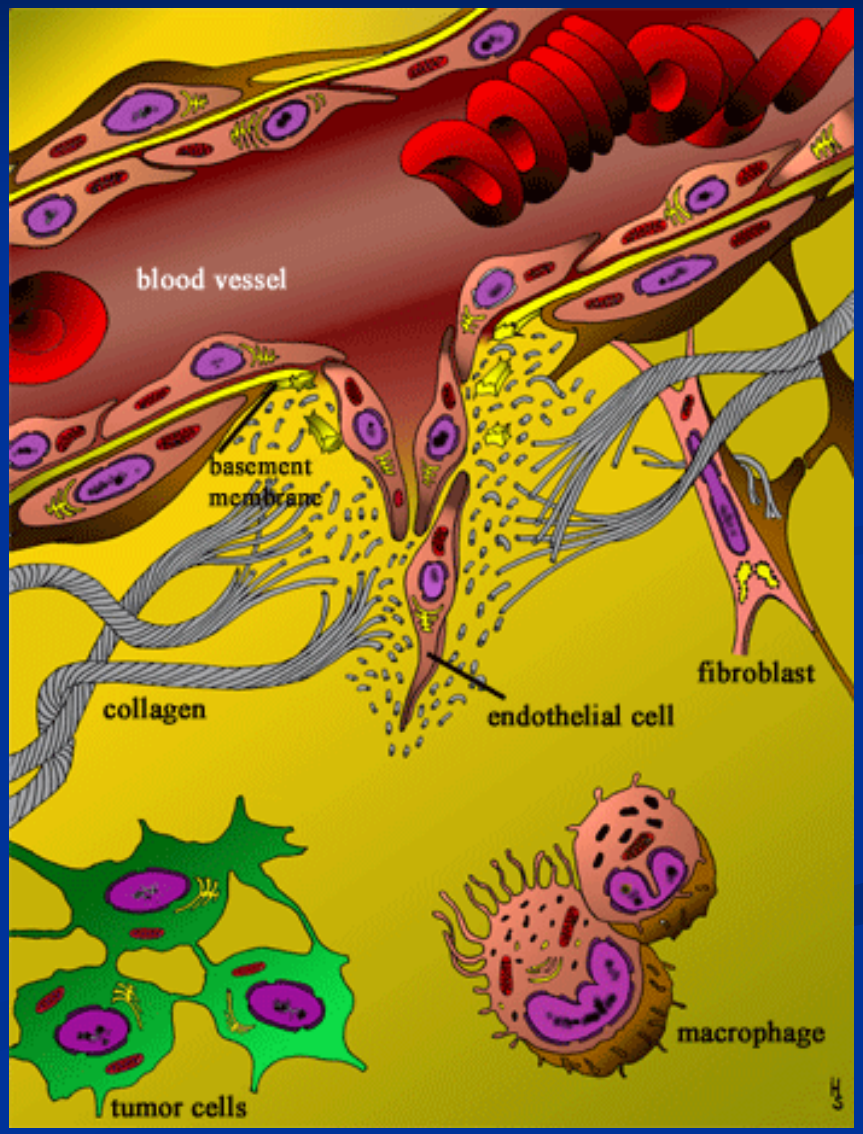
Components of Wound Healing

O2 metabolized

- Stimulates increase in GF
- Stimulates epithelialization
- Granulation tissue formation
- Glycosaminoglycan production
- Collagen synthesis
- NO: antibiotic effect



Witte, M., et al Role of nitric oxide in wound repair. *Am J. Surg.* 183: 406, 2002

Vehicles for Delivery

- Nasal Cannula
- Hyperbaric chamber
- Topical closed chamber (plastic bag)
- Topical transcutaneous injection
- Transdermal sustained O_2 (electrochem rxn)
- Suspension

Vehicles for Delivery

Nasal Cannula/mask

- Systemic O2 inhalation therapy
- Improves tissue oxygen conc
- Optimizes healing and resistance to infection

World J. Surg 2004 Arch Surg 1997

Vehicles for Delivery

Systemic O2 inhalation therapy

Clinical trials:

- Keeping pts warm and
- Admin supplemental O2

- Decreased rate of infection in surgical pts

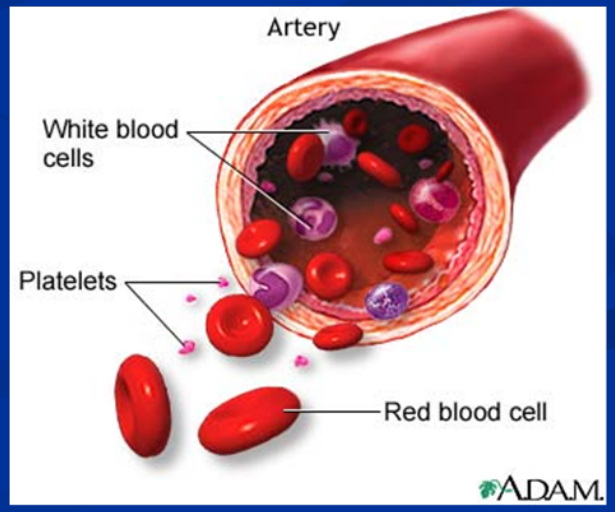
N Eng J Med 1996 N Eng J Med 2000

Oxygen and Wound Healing

Vehicles for Delivery

Hyperbaric chamber

- Introduced by Henshaw
- Extensive use: Military Med
- More common in clin prac
- 2-3 Atmospheres of pressure may carry as much as 5-6 ml dissolved oxygen per 100 ml blood



Ann NY Acad Sci ’65 J Can Med Assoc ’67
Undersea Med Soc ‘79S Oncol ’93 E Med ‘05

HBOT

Early work

Baroni diabetic foot ulcers

16/18 pts in HBOT group healed
1/10 pts in control group healed

Diabetes Care 1987

Oxygen and Wound Healing

HBOT

- Oriani 1990 J Hyperb Med 62 patients
- Zamboni: 1997 J Hyperb Med 10 patients
- Faglia: 1996 Diabetes Care 68 patients

All demonstrated improved healing with HBOT

Oxygen and Wound Healing

HBOT

Niinikoski 2004

- Stimulation of fibroblast proliferation and differentiation
- Increased collagen formation and crosslinking
- Augmented neovascularization
- Stimulation of leukocyte microbial killing

Oxygen and Wound Healing

HBOT

2006 Kranke, Bennet et al

- Review of all published work on HBOT
- Emphasis on randomized trials
- 1° outcome measured: prop ulcers healed
  prop undergoing major amps
- 2° outcome measured: time for complete healing
  wound size reduction
  prop undergoing minor amps

Oxygen and Wound Healing

HBOT

Randomized clinical trials:

- Doctor 1992
- Faglia 1996
- Lin 2001
- Abida 2003

- 2006 Kranke, Bennet et al

Oxygen and Wound Healing

HBOT

Pts requiring minor amps:

- Doctor 1992
- Abida 2003

Result: No Significant reduction in amp rate with HBOT

2006 Kranke, Bennet et al

Oxygen and Wound Healing

HBOT

Pts requiring major amps:

- Doctor 1992
- Faglia 1996
- Abida 2003

Result: Significant reduction in amp rate with HBOT

2006 Kranke, Bennet et al

Oxygen and Wound Healing

HBOT

Abida 2003 Proportion of ulcers healed

18 patients randomized 9/9

- wounds treated 6 weeks: no sig healing
- wounds treated 6 months: no sig healing
- wounds treated 1 year: significant healing

2006 Kranke, Bennet et al

Oxygen and Wound Healing

HBOT

Absolute Transcutaneous O2 Tension in affected foot

- Faglia 1996
- Lin 2001
- Abide 2003

TCOT was significantly higher in pts treated with HBOT

- 2006 Kranke, Bennet et al

Vehicles for Delivery

Topical oxygen therapy (int)

- Topical closed chamber
- (polyethylene bag)
- Sometimes referred to HBOT, or THOT
- Variable outcomes
- Many reports anecdotal

OWM '02, J Pathophys '03,
JAPMA 1985, JFS 1987 Phys Ther '86

THOT v SWC

- Prospective randomized study
- 40 patients 79 necrotic/gangrenous wounds
- THOT 1.004 to 1.013 atm

- Results: 90% wounds healed THOT group
  22% wounds healed SWC controls
- Conclusion: THOT stim angiogenesis with
  enhanced healing nec wounds

Ostomy Wound Manage. Sept 2000

THOT

"Validity of many reported outcomes has often been refuted, based on a variety of parameters."

Am J. Dermatol 1986

THOT

"Healing is not enhanced …"

Diabetes Care 1988

Topical Transcutaneous Injection

- Intermittent exposure to O2 injection; Vessel formation
  Ligamentous tear. 17 male rats
- 1 Control
- 2 Inj Hyaluron+ Hb + O2

- Res: Vessel form: Promoted Group 2, Lower in control group
  VEGF mRNA was lower in Group 2 , higher in control g 1

- Conclusion: O2 accelerates vessel formation
  in spite of its effect of dec VEGF mRNA

J Orthop Res. 2003

TOE Topical Oxygen Emulsion

- Supersaturated O_2 suspension
- Perfluorocarbon components
- Double blind randomized controlled study
- 2nd, 3rd degree burns

- Results: TOE enhances rate of epithelialization

Arch Dermatol 2007

Oxygen and Wound Healing

Topical Oxygen

- Induces Vasc Endo Growth Factor Expression
- Improves Closure of Chronic wounds

Clinical and Experimental Pharm and Physio 2008

TO v HBO Therapies

- 1854 pts screened for non randomized enrollment
- TO n=25 (52%DM) HBO: n=32 (31% DM)

- Results: 1. HBO "seemed to benefit some, not others"
  no stat significant improvement: wound size

  2. TO: "significantly improved wound size

Clinical and Experimental Pharm and Physiol 2008

VEGF, TGFB1, and COLIAI

Specifically, 3 O_2 Sensitive genes were studied:

Result:

Higher VEGF165 expression in healing wounds

Established a link between VEGF gene expression and healing outcome for TO therapy

(no sig inc expression of any genes with HBO)

Topical Oxygen

- Intermittent Oxygen Delivery:

  90 minutes /day pure O2 4 days out of a week.

- Sustained Oxygen Delivery: New Technology

  Transdermal Cutaneous OxygenTherapy

Topical Oxygen: Vehicles for Delivery

- Transdermal sustained O2 Therapy
- Generator delivers O2
- 3ml/hour of pure O2/hr
- Continuous flow
- Occlusive dressing

Transdermal Sustained O2

Said et al 2005

- Controlled clinical trial rabbit model and small punch biopsy wound on the ears.
- Result: improved healing 5-8 days, increased epithelialization as compared to control

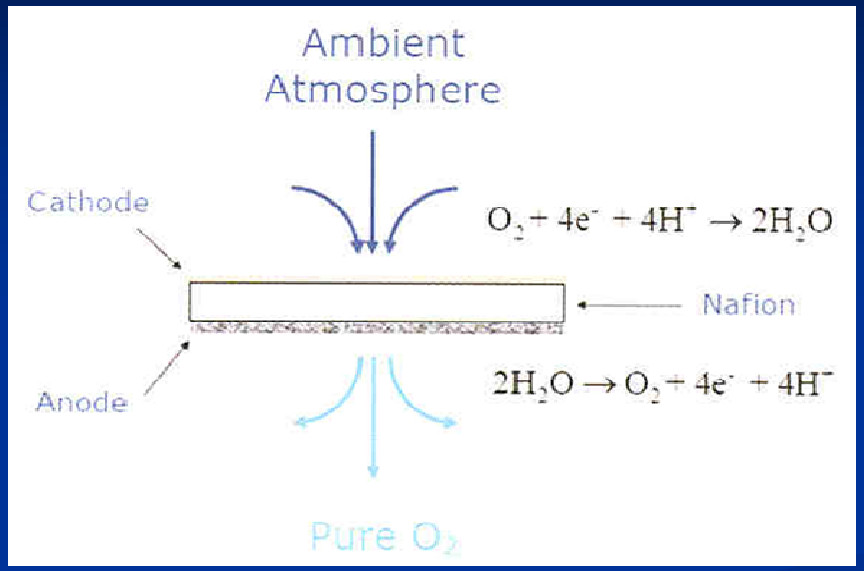
Archives of Surgery 2005

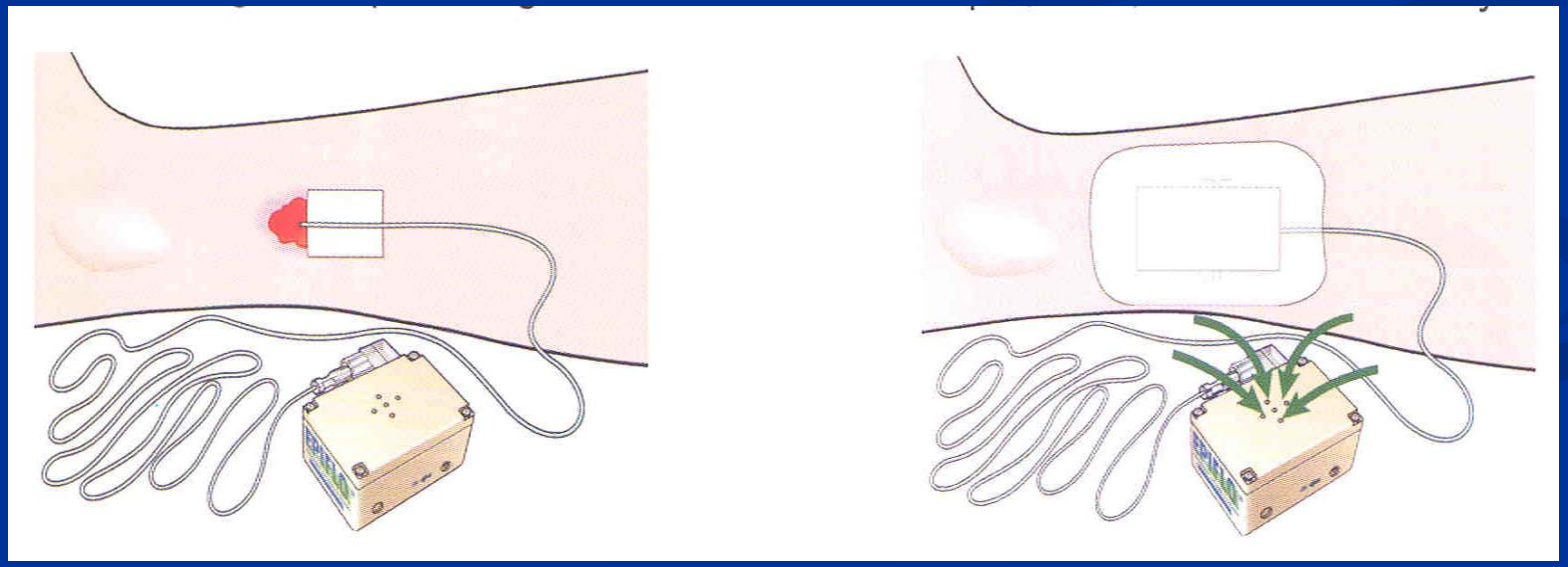
Transdermal Sustained O2

- 3 case studies
- Large Stage IV pelvic pressure ulcers
- 5 weeks: significant healing, reduction of wound size

J Spinal Cord Med 2008

Tech: O_2 is Extracted from Ambient Air





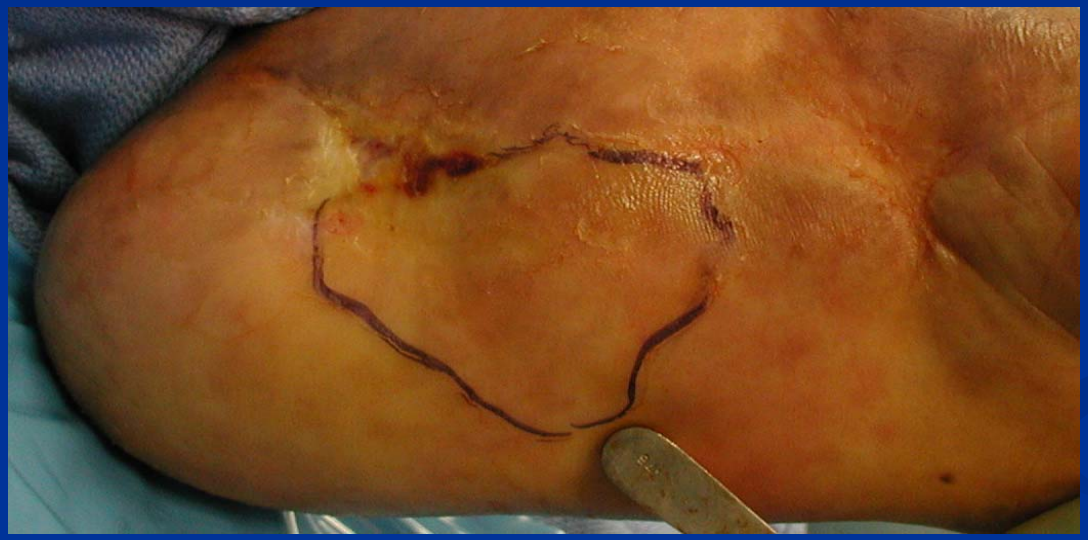
Sustained Delivery

Case Presentations

Case #1:

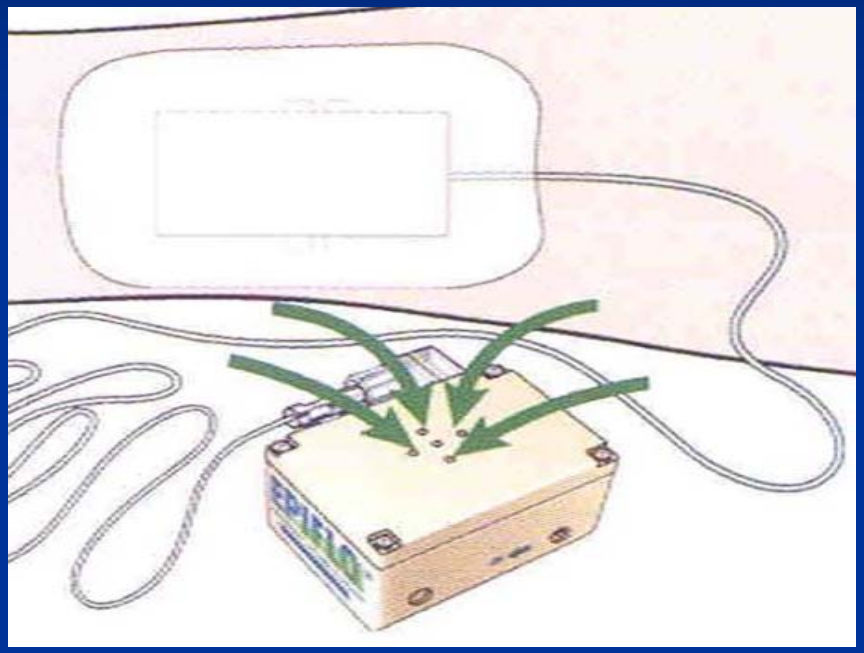
- ER 71 yo AAM
- Foot crushed 1962
- Bone: mult fusions
- Skin: hypertrophic scar
- Non-healing ulcer
- ***EXTREME* PAIN**
- **Patient unable to wb**

Case #1 Initial Treatment



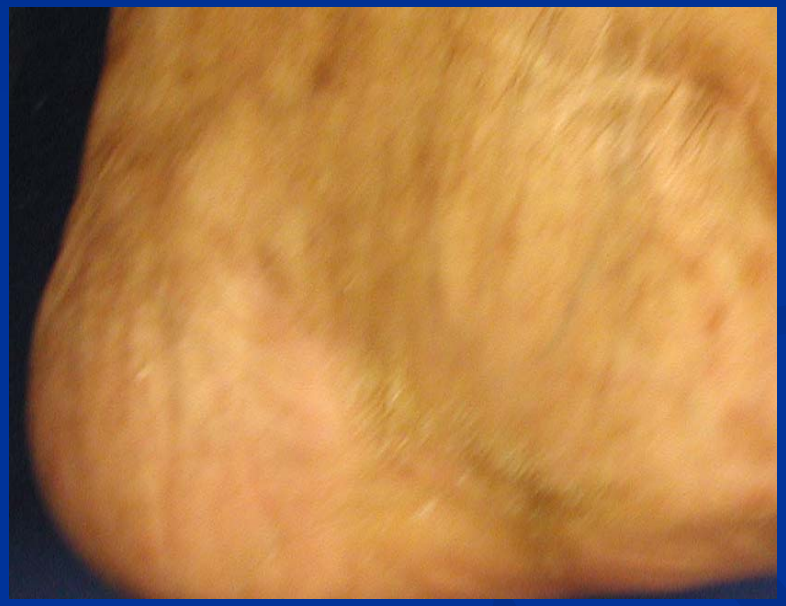
Patient taken to OR: Scar Revision, Debridement

Case #1 Extended Treatment



Transdermal Sustained Oxygen Delivery

Case #1 OUTCOME



Case #2: 48 yo male

Major dehiscence/breakdown of surgical wound

Case #2:

- 48 year old male pt
- SP Trauma/assault
- Pt: Incomplete quadriplegic
- Adult acquired clubfoot
- Chronic ulcerations

- **Underwent clubfoot sx**

Case #2 Initial Treatment

- Patient underwent Clubfoot repair
- Release TA, FHL, FDL, PT
- Release TNJ, STJ, AJ
- Partial excision of talus
- Ankle arthroplasty

2 weeks post op, wound breaks down

Wound: non responsive to wound care
Transdermal sustained O2 therapy added

Case #2 OUTCOME

Case #3

Case #3 Non Healing ulcer

- 64 year old male
- Vietnam Vet
- Combat injury: grenade
- Chronic non healing
- >35 years
- EXTREME PAIN

Conventional wound care failed to heal, sustained transdermal O2 therapy was added

Case #3 OUTCOME

Case #4

- 56 year old male
- CAD, HTN, PVD,
- Sp DVT Fem/Fem
- 85 year pack hx tob
- Chronic Ulceration 4yr
- Medial malleolus
- SP trauma
- PVD
- EXTREME PAIN

Case #4 Extended Treatment

Case #4 OUTCOME

SUMMARY

SUMMARY

- Hypoxia limits wound healing

SUMMARY

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- Oxygen has a role as a nutrient and antibiotic, and influences gene expression for dev of growth factors

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- Correcting a compromised state of tissue O2…through administration of sup O_2 benefits wound healing

SUMMARY

- Hypoxia limits wound healing
- Oxygen has a role as a nutrient and antibiotic, and influences gene expression for dev of growth factors
- Correcting a compromised state of tissue O2 through administration of sup O2 benefits wound healing
- Supplemental oxygen may be provided through nasal cannulas, hyperbaric or topical delivery systems.

SUMMARY

If Considering Supplemental Oxygen Therapy

- Patient Selection and Wound Parameters

SUMMARY

If Considering Supplemental Oxygen Therapy

- Patient Selection and Wound Parameters
- Caution with possible risks, adverse effects, toxicity, availabililty, pt compliance and costs

SUMMARY

If Considering Supplemental Oxygen Therapy

- Patient Selection and Wound Parameters
- Caution with possible risks, adverse effects, toxicity, availabililty, pt compliance and costs
- Research: Evaluate the Evidence.

With Supplemental Oxygen Therapy

More studies are needed in the form of randomized controlled clinical trials.

Thank you