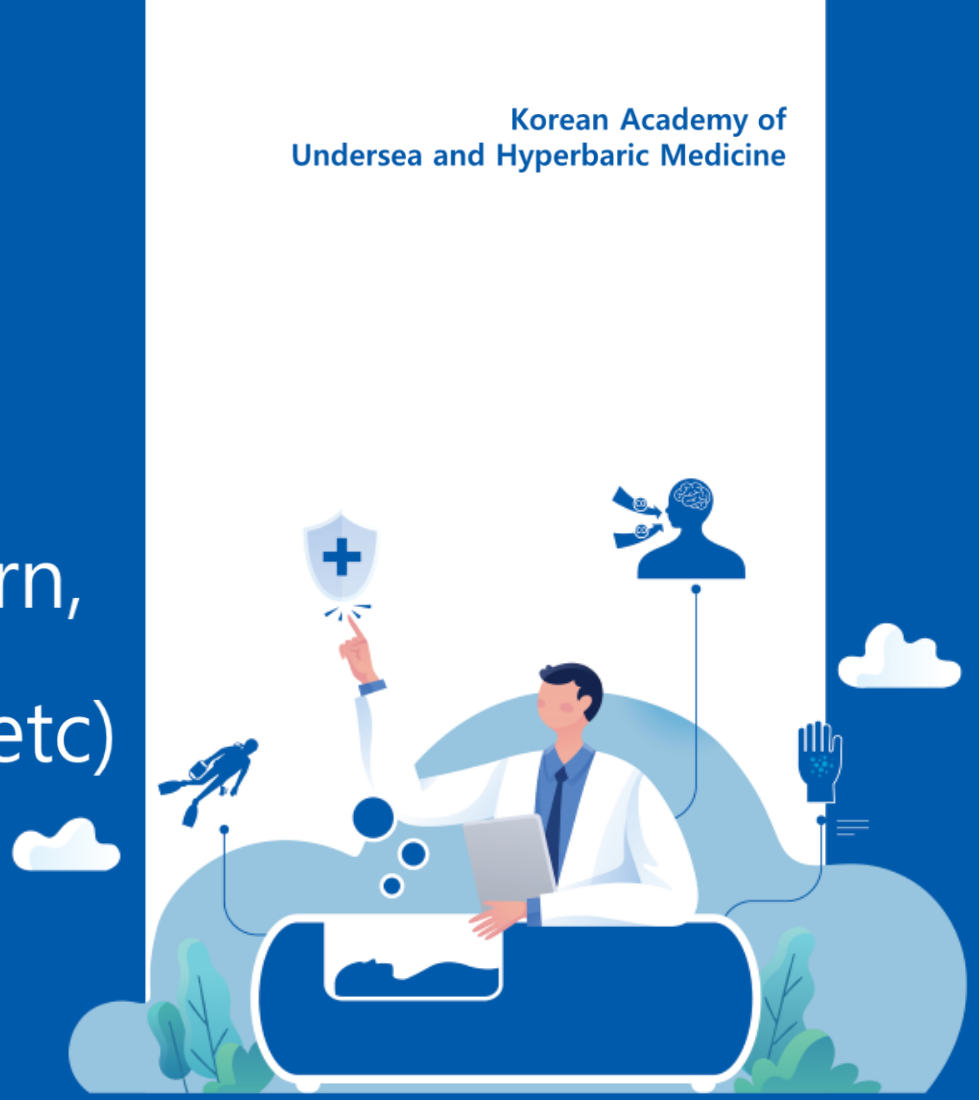
Emergent HBOT for traumatic injury to disease related wounds

(amputation, compromised flap, burn, necrotizing fasciitis, gas gangrene, etc)



2021.10.21(목)

소 속 : 전남대학교병원 응급의학과
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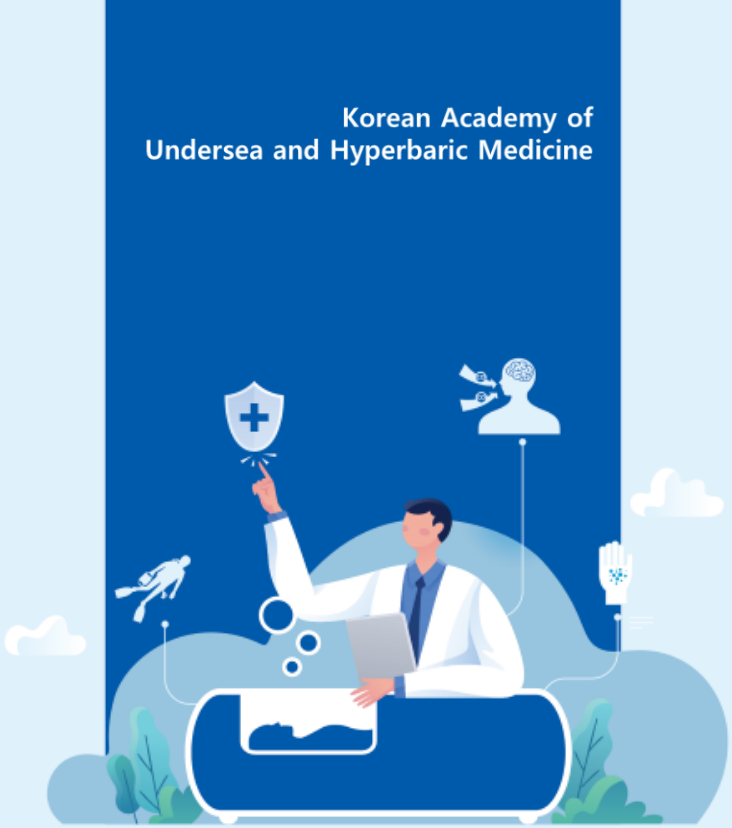
I HBOT 기전 (상처 치유)



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〈보험 적용 적응증〉

가)군 응급 치료	나)군 만성 상처 치료	다)군 기타
• 일산화탄소중독 • 감압병(잠수병) • 가스색전증 • 혐기성세균감염증(가스괴저증) • 시안화물중독증 • 급성 중심 망막 동맥폐쇄 • 수혈이 불가능한 경우의 과도한 출혈에 의한 빈혈	• 화상 • 버거씨병 • 식피술 또는 피판술 후 • 수지접합수술 후 • 방사선치료 후 발생한 조직괴사 • 당뇨병성 족부궤양 • 난치성 골수염 • 머리 농양	• 돌발성난청

〈보건복지부, 2019. 01〉

HBO 급여기준

건강보험심사평가원

적응 증	기존 횟수	개선안	비고
일산화탄소/시안화물 중독	제한 없음	14	DNS 발생시 +40
감압병	제한 없음	14	신경증상 +20
공기 색전증	제한 없음	7	신경증상 +20
가스괴저증	제한 없음	7	
식피 술/피판 술/수지 접합 후 탈락 위험	14	20~	필요에 따라 증가
화상	14	30~	필요에 따라 증가
말초 허혈증 (버거씨 병)	14	30~	필요에 따라 증가
지연성 방사선 손상	14	30~	필요에 따라 증가
돌발성난청(70 Db 이상)	제한 없음	20~	필요에 따라 증가
압착 손상과 구획 증후군	14	14	필요에 따라 증가
중증 빈혈	제한 없음	30~	필요에 따라 증가
괴사성 연부조직염	14	7~	필요에 따라 증가
골수염, 당뇨발	14	21~	필요에 따라 증가
뇌내 농양	14	40~	필요에 따라 증가

Mechanisms of HBOT

Primary mechanism	Secondary mechanism
Hyperoxygenation Pressurization (Bubble reduction)	Vasoconstriction Host response Microbiological Effect Impede Reperfusion Injury Gas Washout

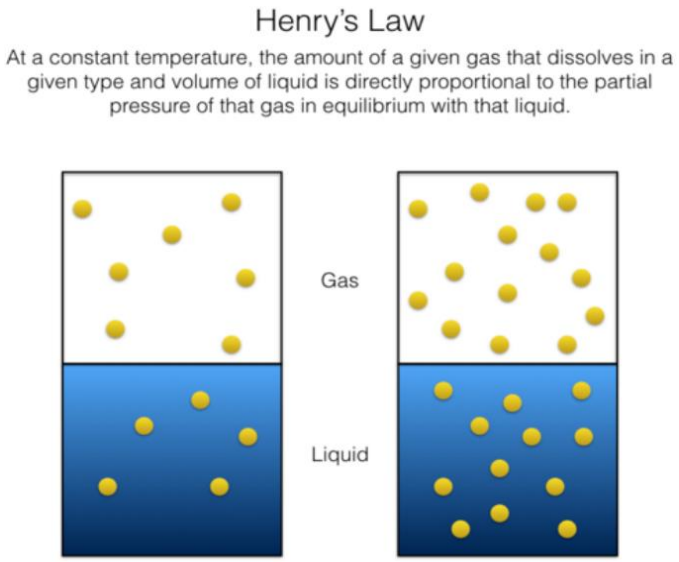
즉각적 효과

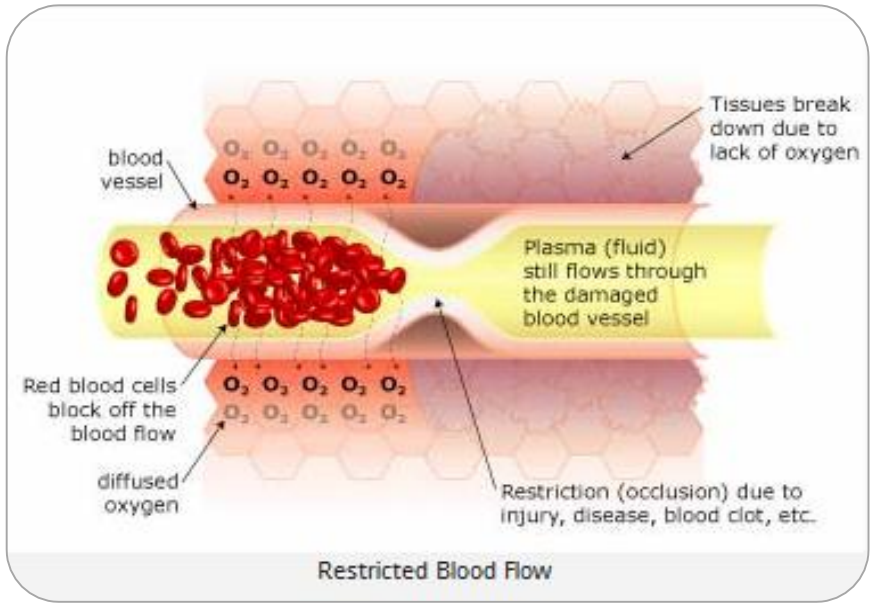
고농도 산소 효과의 누적

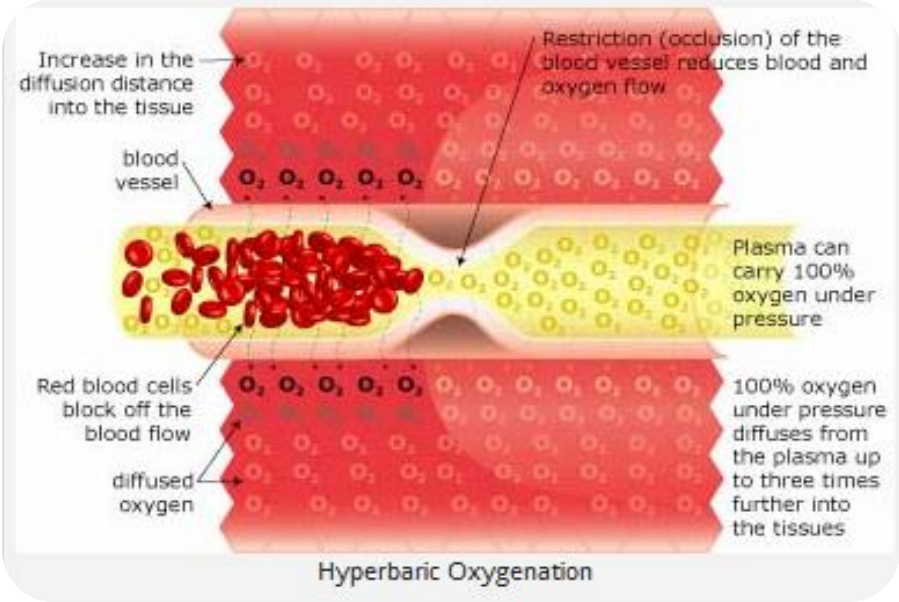
Wound care를 설명

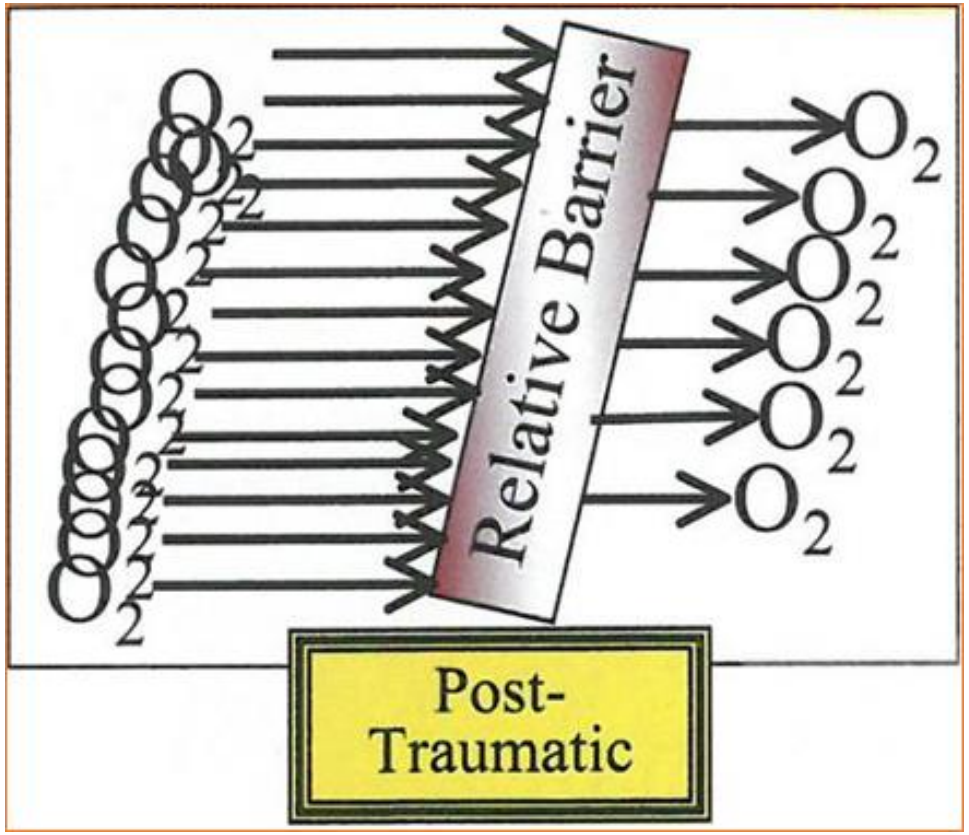
Hyperoxygenation (Primary mechanism)

- 고압환경에서 100% 산소를 공급, Plasma와 Tissue fluid의 산소양을 증가
- 모세혈관에서의 산소 확산률 증가 -> 다양한 barrier를 쉽게 통과 – 2ATA 환경, 기존 대비 3배 확산률





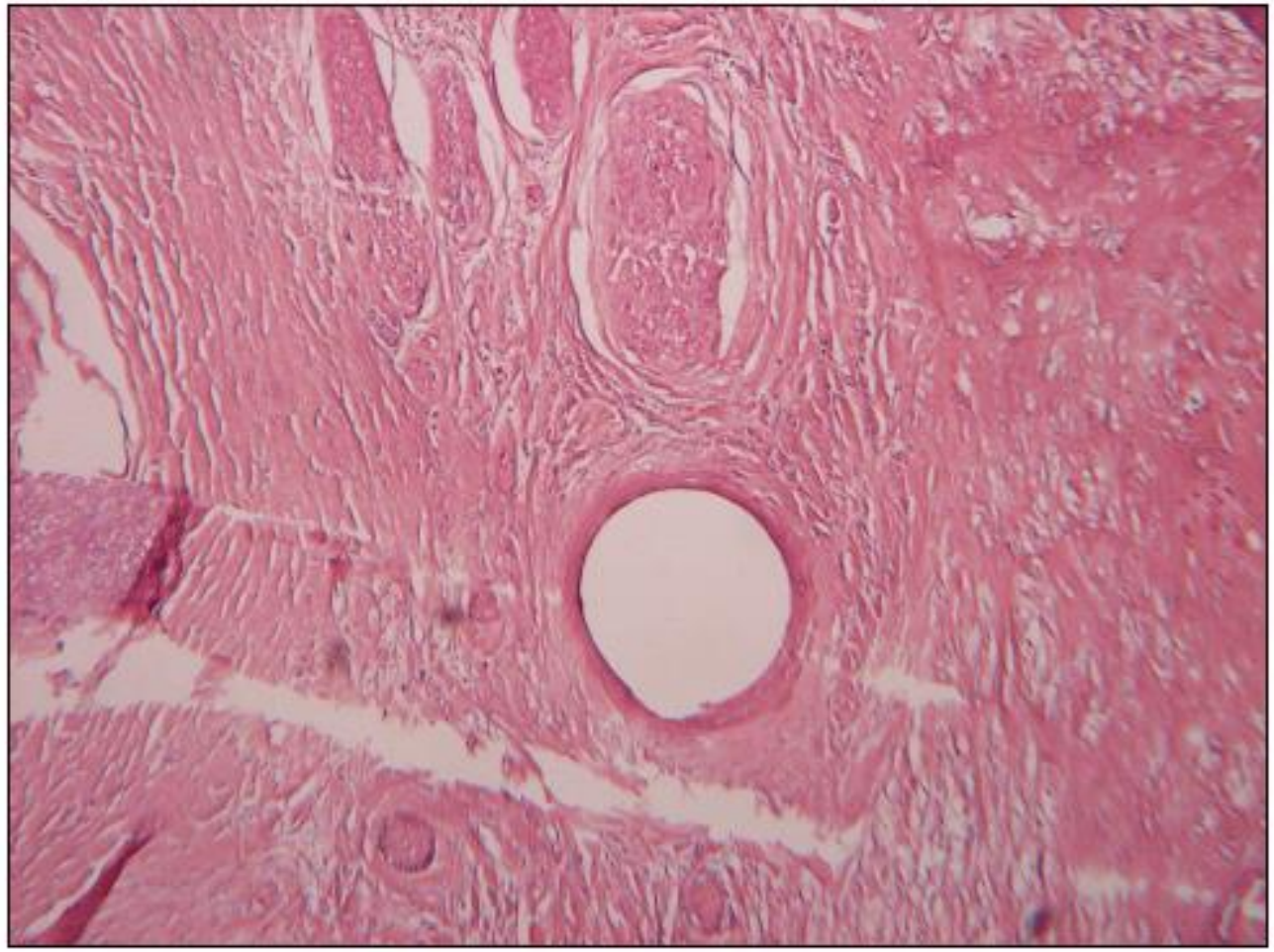




1/2

3H Tissue

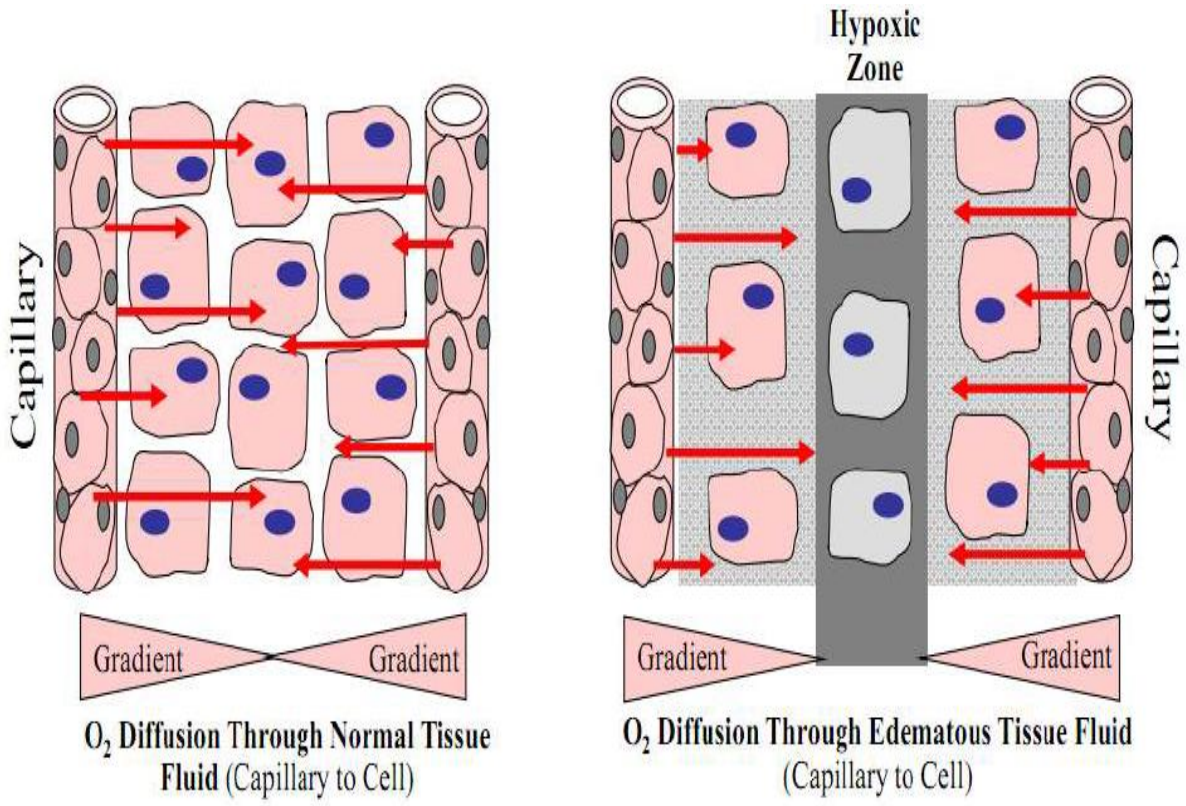
- Hypovascular
- Hypocelluar
- Hypoxic



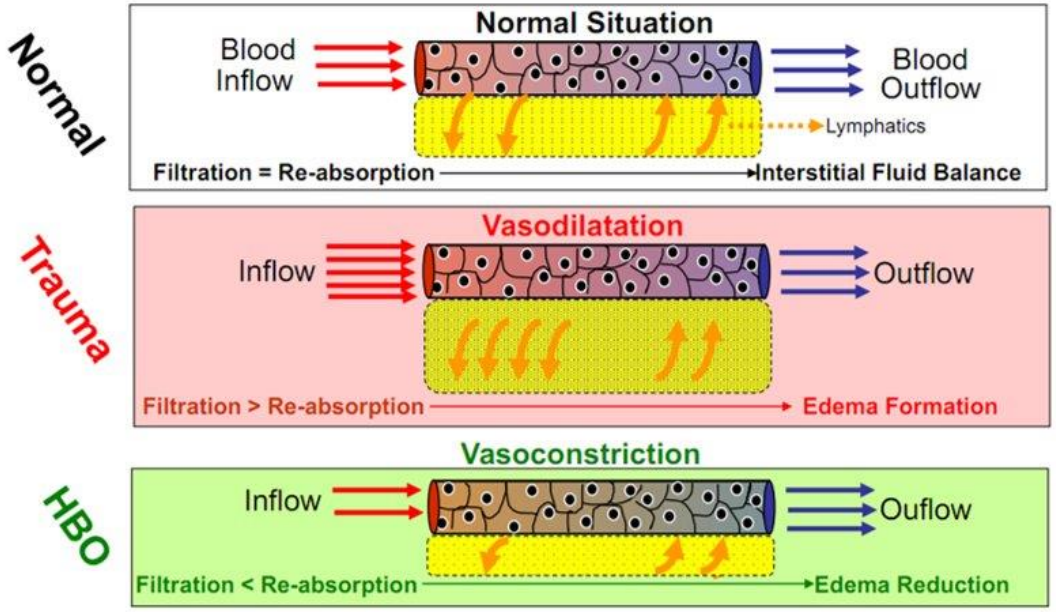
Hyperbaric medicine practice 4th edition

Vasoconstriction (Secondary mechanism)

- 혈관 수축 -> Edema reduction
- 혈류량이 감소하더라도 Plasma, tissue내의 O2 농도는 높게 유지 -> Hypoxic zone의 O2 diffusion



Vasoconstriction

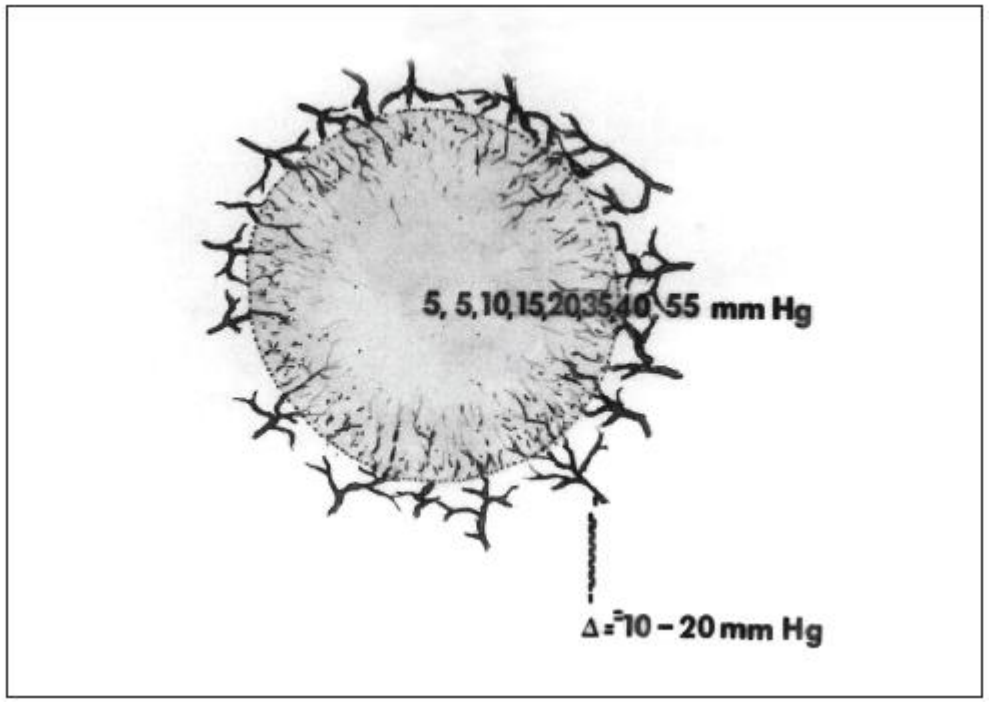


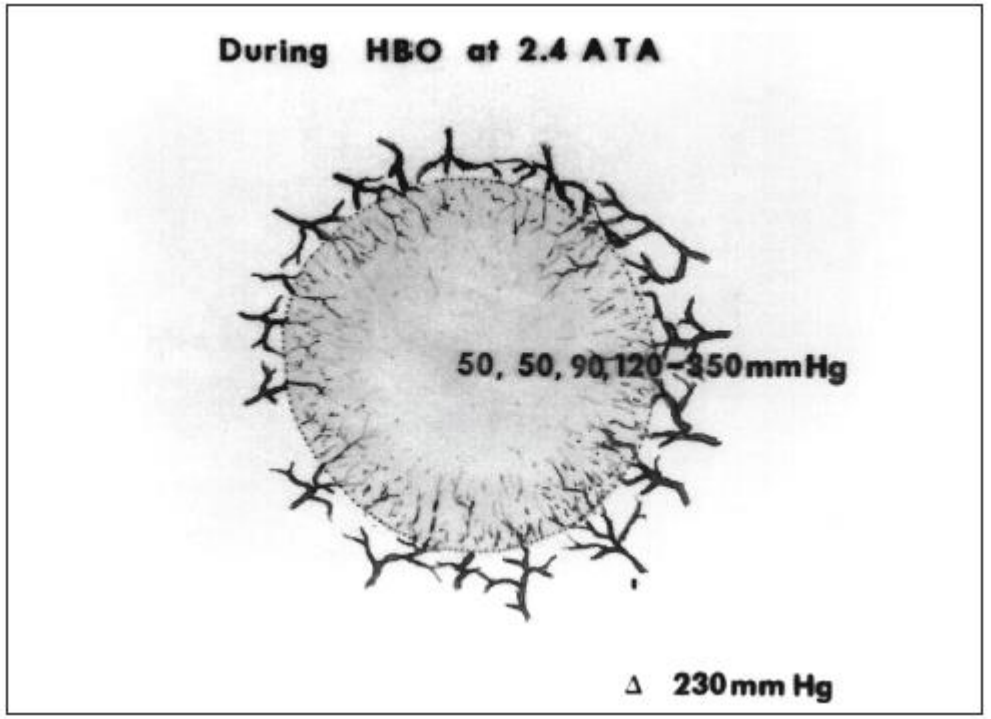
20%

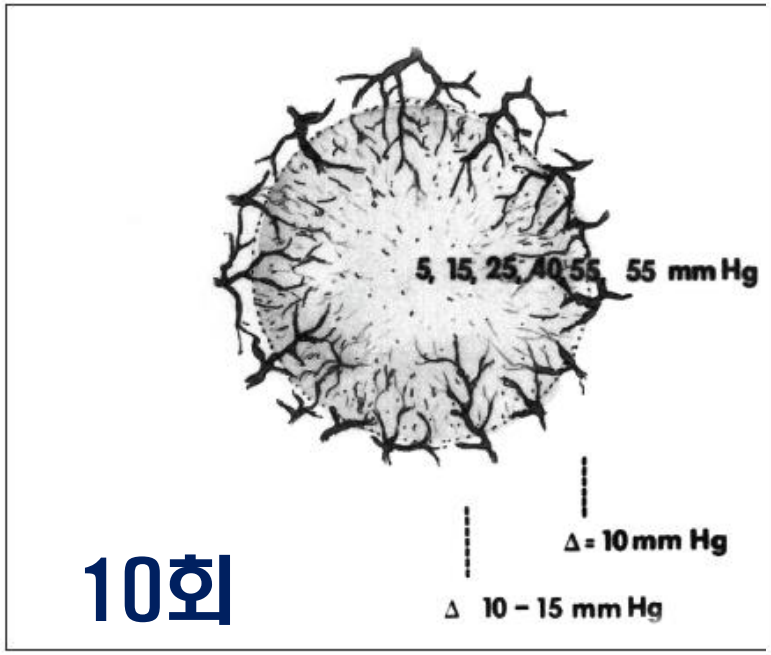
Host response (Secondary mechanism)

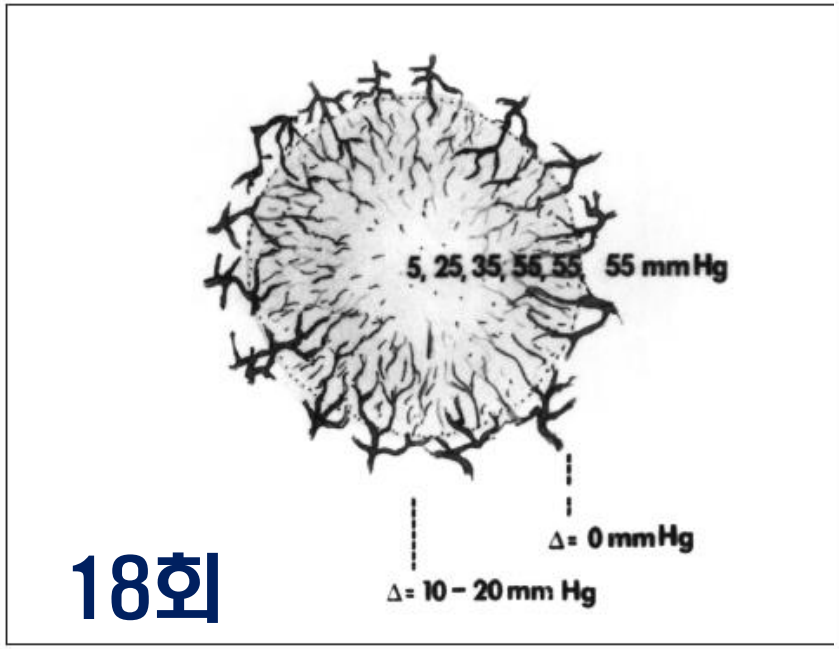
3 oxygen dependent host cells related to wound healing and infection control

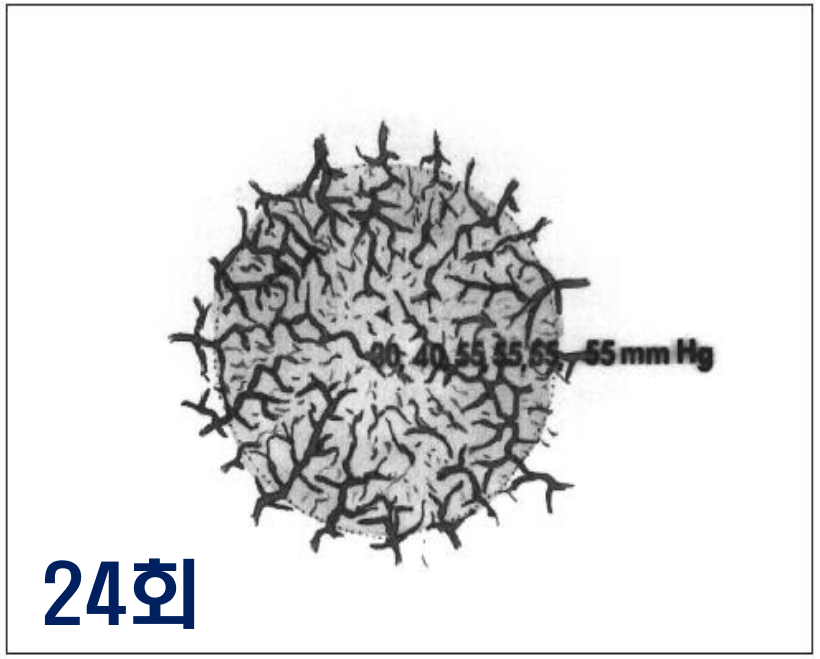
- **Fibroblast (associated with angiogenesis)**
- **Neutrophils (WBC oxidative killing)**
- **Osteoclasts**


5, 5, 10, 15, 20, 35, 40, 55 mm Hg
Δ ≈ 10 – 20 mm Hg


During HBO at 2.4 ATA
50, 50, 90, 120 – 350 mm Hg
Δ 230 mm Hg







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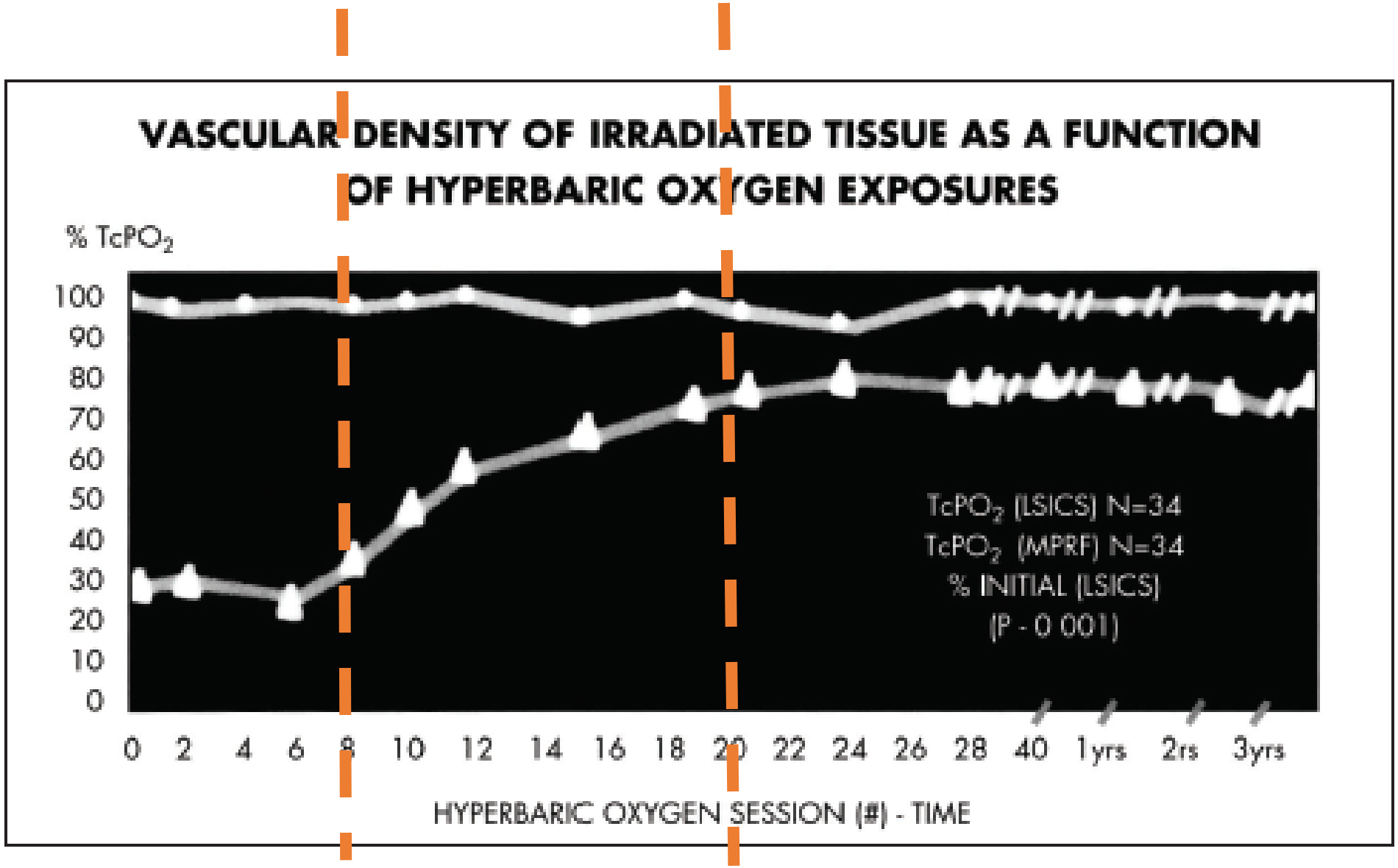


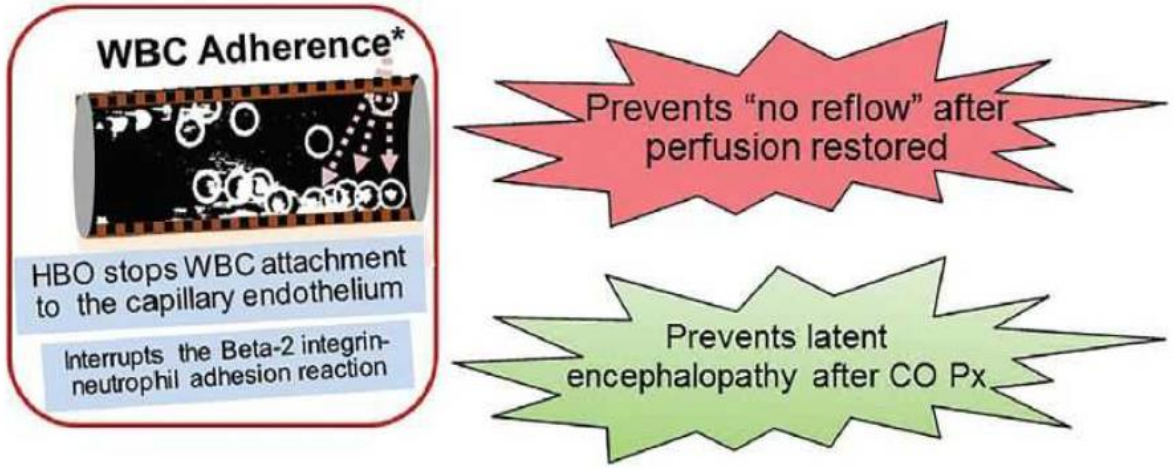
Hyperbaric medicine practice 4th edition

Microbiological effects (Secondary mechanism)

- Bacteriostatic and bacteriocidal effects
  - ≫Clostridial organisms (no killed but stop multiplying)
  - ≫Anaerobic streptococcus and peptostreptococcus are killed by hyperoxic condition
  - ≫Bacteroids species killed by hyperoxia
  - ≫Fungal infection by actinomyces species
- Cessation of the endotoxin formation produced by clostridial organisms
- Toxin inactivation has been best appreciated with the theta toxin produced by clostridial organisms
- Additive effect with certain antibiotics
  - ≫Aminoglycosides
  - ≫Amphotericin
  - ≫Possibly vancomycin

Mitigation of reperfusion injury

- Interrupt the neutrophil adherence to the endothelium by beta-integrin attachment mechanism inactivation
- Extreme hyperoxia environment triggers to generate oxygen free radical scavengers (superoxide, peroxidase)



LEGEND: Mitigation of neutrophil adherence to the capillary endothelium sensitized by hypoxia reduces/eliminates the release of toxic O_2 radicals (peroxides and superoxides) that cause the harmful effects of the reperfusion injury.

In addition, this prevents the cascade of reactive oxygen species with nitric oxide (NO)--in hypoxic environments--from forming highly toxic degradation products such as peroxynitrite (-OON).

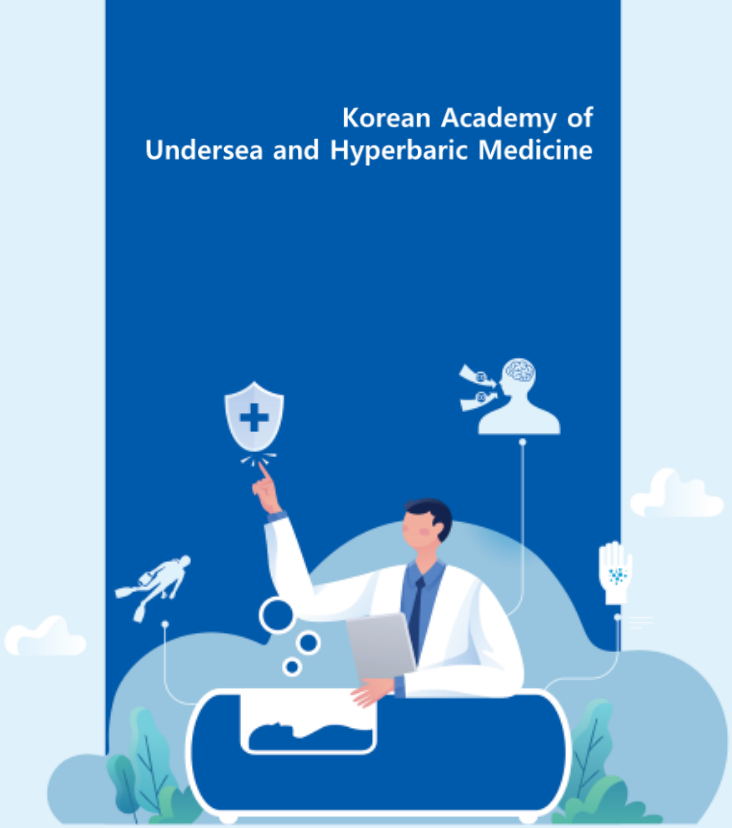
NOTES & KEY: *Neutrophils adhering to the sensitized capillary endothelium are so indicated by white circles around them (Zamboni[10]); CO Px = Carbon monoxide poisoning, HBO_2 = Hyperbaric oxygen, WBC = White blood cell

Figure 35. Morphology of the reperfusion injury and roles of HBO_2 in mitigating its effects.

- Recommend starting HBO as soon as possible after an extended period of ischemia in critical tissue such as the brain and heart as well as skeletal muscles and perhaps in other organs such as the liver, kidney, pancreas, etc.

- HBO should be considered after revascularization surgeries associated with long ischemia times
  - Re-implantations
  - Threatened flaps
  - Other situations where there is a possibility that reperfusion injury will contribute to more morbidity.

Ⅱ 급성기 창상



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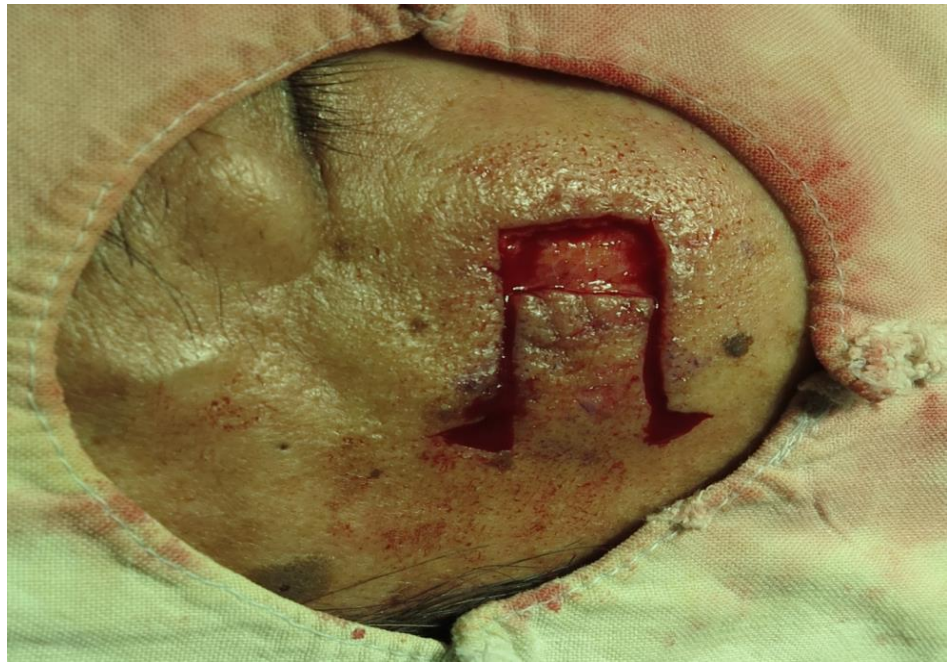
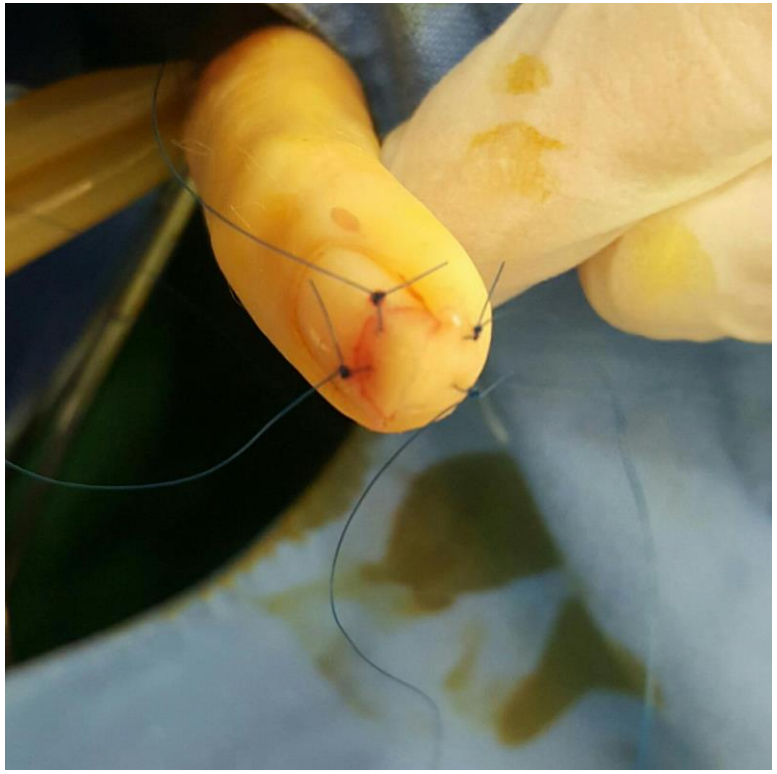
Flap



Graft

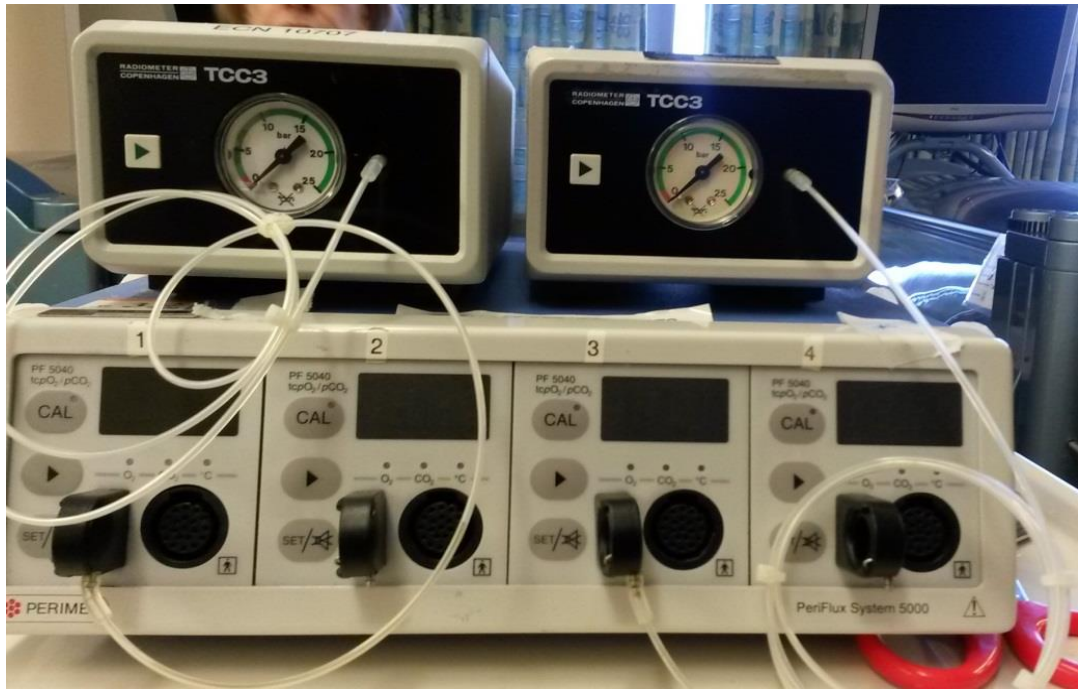
Graft



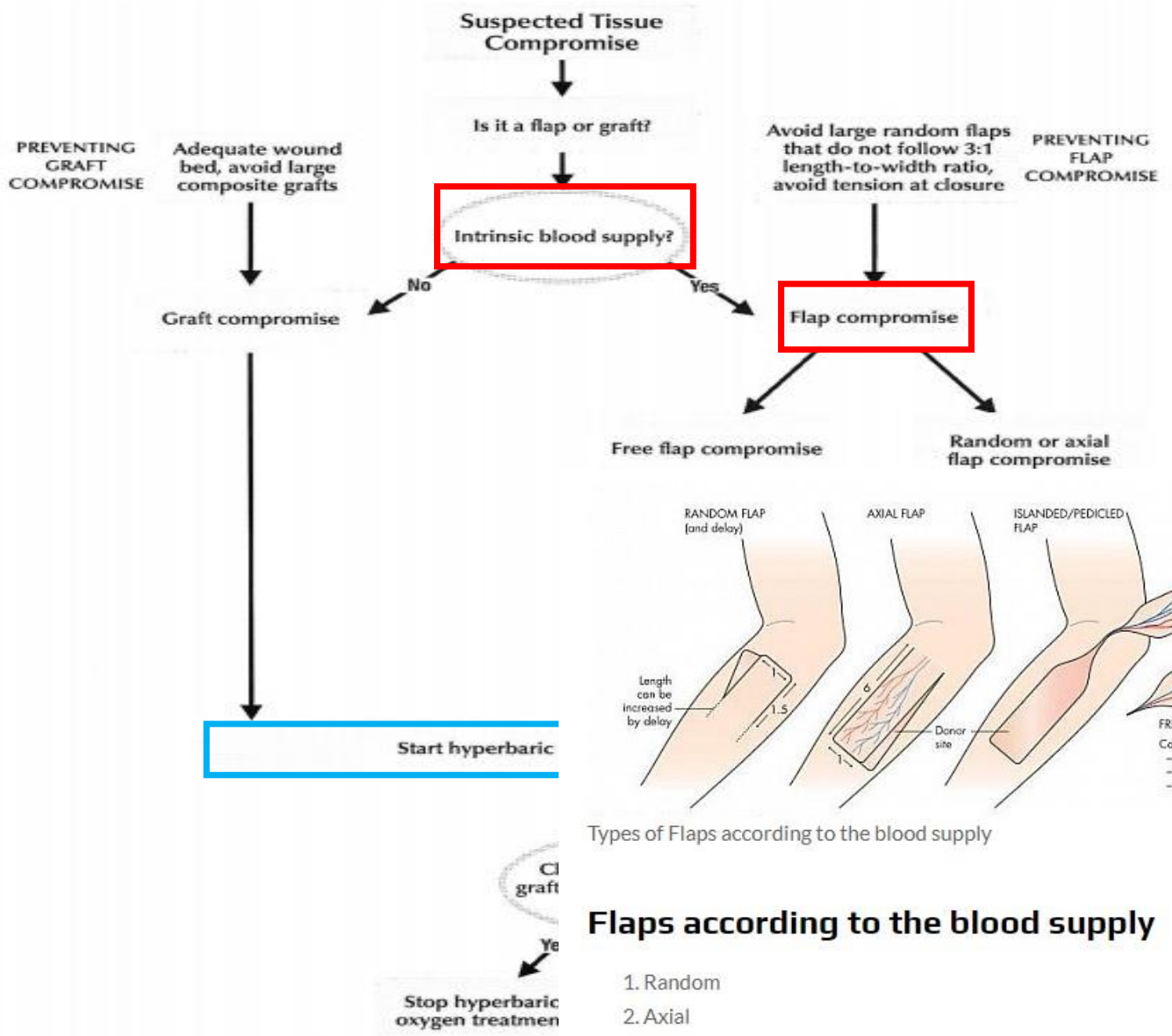
Compromised Flap

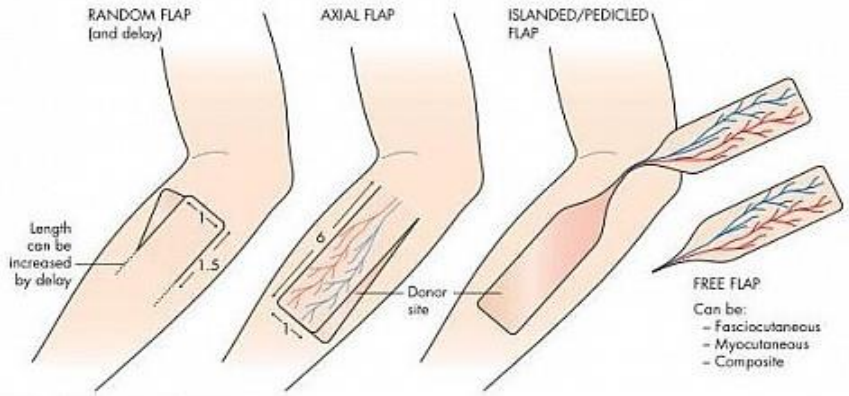
Measurement of Wd. hypoxia

Transcutaneous oxygen tension (PtcO2) : most useful



PtcO2 < 40mmHg : HBOT





Types of Flaps according to the blood supply

Flaps according to the blood supply

1. Random
2. Axial
3. Islanded or Pedicled

Protocol

- 2~2.5 ATA
- 90~120 min
- Initial : 2/day
- Stable / viable : 1/day

Compartment syndromes

CLINICAL CASE REPORT

Successful adjunctive treatment of compartment syndrome due to acute isocyanate inhalation using hyperbaric oxygen therapy: case report

Sungmin Lee, MD; Junho Han, MD; Tag Heo, MD PhD

Department of Emergency Medicine, Chonnam National University Medical School, Dong-gu, Gwangju, Republic of Korea

CORRESPONDING AUTHOR: Tag Heo – *terran034@gmail.com*

ABSTRACT

Introduction: Isocyanates are the raw materials that make up all polyurethane products. Isocyanate is a powerful irritant to the mucosal membrane of the respiratory tract, eyes and skin. Pulmonary symptoms, especially occupational asthma, are predominant manifestations of isocyanate toxicity.

Case report: We report mental changes and compartment syndrome complicated with rhabdomyolysis as an extraordinary manifestation of acute isocyanate toxicity observed in a patient during the waterproofing of a water tank. A 58-year-old man recovered consciousness after six hours in the emergency department and complained of severe pain in the lower leg. The results of his laboratory test showed that his serum creatine kinase (15,250 IU/L) level had increased. The tissue pressure in both the lower legs had increased to 180 mmHg/170 mmHg (right/left).

We performed fasciotomy on the second day of hospitalization. The patient was provided hyperbaric oxygen (HBO_2) therapy of 2.0 ATA for 90 minutes twice a day for seven days. His condition gradually improved over five months, and he did not require amputation. He had a mild neurological disorder in his foot and was transferred to a rehabilitation center five months after hospitalization.

Conclusion: It is important to note that when working with isocyanate, non-specific complications such as a change in consciousness as well as compartment syndrome with rhabdomyolysis can occur in a confined space or high-temperature environment. In addition, we found that compartment syndrome caused by isocyanate toxicity can be effectively treated with fasciotomy and HBO_2 therapy. ▮

Figure 1. Both legs after fasciotomy (A: right, B: left)

Table 2. Acute findings of lower leg physical exam and tissue pressure

(Rt/Lt)	HD 1	HD2 (07:00)	HD2 (15:00)	HD2 (23:00)	HD3	HD3	HD3	HD4	HD7
pain	(+/+)	(+/+)	(+/+)	(+/+)	(+/+)	(+/+)	(+/+)	(+/+)	(+/+)
pallor	(-/-)	(-/-)	(-/-)	(-/-)	(-/-)	(-/-)	(-/-)	(-/-)	(-/-)
paresthesia	(+/+)	(+/+)	(+/+)	(+/+)	(+/+)	(+/+)	(+/+)	(+/+)	(+/+)
pulselessness	(-/-)	(-/-)	(-/-)	(-/-)	(-/-)	(-/-)	(-/-)	(-/-)	(-/-)
paralysis	(-/-)	(+/+)	(+/+)	(+/+)	(+/+)	(+/+)	(+/+)	(+/+)	(+/+)
tissue pressure	130mmHg/ 130 mmHg	180mmHg/ 170 mmHg	135mmHg/ 125 mmHg	160mmHg/ 160 mmHg	100mmHg/ 75 mmHg	120mmHg/ 80 mmHg	90mmHg/ 90 mmHg	41mmHg/ 70 mmHg	40mmHg/ 55 mmHg

Figure 2. Flaps in both lower legs after four months (A: right; B: left)

Crush injury, Compartment syndromes

Table 3. Treatment Recommendations and Peer Review when Using HBO_2 for Crush Injury and Compartment Syndrome

Conditions	HBO_2 treatments & peer review[1]	Comments
Primary Conditions		
1. **Reperfusion injury**	**1**	Minimal tissue trauma, e.g. after free flaps, revascularizations and transient edema.
2. **Crush injury**	**8** (TID 2 days, BID 2 days and daily 2 days)	If deterioration noted when HBO_2 treatments are decreased, resume the previous schedule.
3. **Compartment syndromes**	**3** (BID day 1 and single HBO_2 treatment day 2)	HBO_2 is not a substitute for fasciotomy; use it for the impending stage of the SMCS.
Residual Problems and/or Complications		
1. **Threatened flaps and grafts**	**14** (BID for 7 days)	If site remains tenuous, considered an additional week of BID HBO_2 treatments.
2. **Problem wounds/infected wounds**	**21** (BID for 7 days, daily for 7 days)	Refer to Chapter 2B Problem Wounds in this Committee Report.
3. **Refractory osteomyelitis**	**21** (Daily for 21 days; possible extension to **40** treatments)	HBO_2 must be integrated with a combined antibiotic & strategy
4. **Post-fasciotomy concerns after SMCS**	**14** (BID for 7 days)	Concerns include massive swelling, threatened flaps, unclear demarcation, neuropathy, etc.

Notes: [1]Peer review should be done by two or more of the following: 1) HBO_2 Consulting physician, 2) Trauma/orthopaedic surgeon managing the case and/or the patient's primary care physician.

Abbreviations: **BID** = Twice a day, **e.g.** = For example, **etc.** = et cetera, **HBO_2** = Hyperbaric oxygen, **SMCS** = Skeletal muscle-compartment syndrome, **TID** = Three time a day

Thermal burns

Figure 11. Burn Victim's Recovery

A. 23-year-old white female with facial burns from flaming gasoline and tar 12 hours after injury.

B. 24 hours later (36 hours after injury) after two HBO_2 treatments. Note resolution of edema.

C. 72 hours later (84 hours after injury) after six HBO_2 treatments.

D. Shortly before discharge.

E. Four years after discharge.

Note: Consent to use these photos was obtained prior to publication.

HBOT on Burn wounds?

- Inflammatory Cell Reduction
- Angiogenesis
- Increased Epithelialization

Indications

- Burns that extend into the dermis and beyond
: 2nd / 3rd degree

- Inhalation burn

- Impaired wound healing

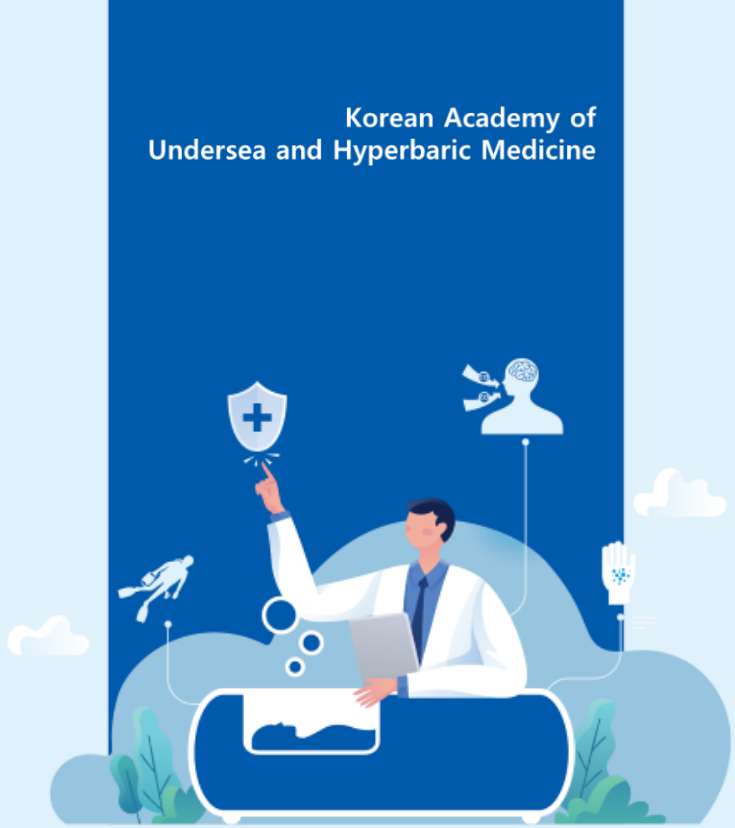
- Extensive edema

- A large skin area envolved

Techniques

- As soon as possible !!
- 1st 24hr : 3 times : 90min with 2.0~2.4 ATM
- 2nd day ~ : twice / day
- total 20~30 sessions.
- No. of treatments : wound response and extends

Ⅲ 연조직 괴사 감염(Necrotizing soft tissue infection)



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개 요

- Aerobic / Anaerobic / Mixed bacterial floras

- Immune-compromised
  - Underlying systemic disease
    - DM, malignancy, vascular insufficiency, alcoholism
  - Transplantation : immunosuppressive drug
  - Neutropenia

- After trauma
- Surgical wound : around foreign body
- Spontaneously : *i.e.* Fournier's gangrene
- Post op. : C-sec (without risk factors), even after "sterile" op.

suspicion

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Epidemiology

- 미국의 경우 한해 약 500-1,500건의 괴사성 연조직염이 발생(10만명 당 4건) , 8-65%(평균 21.9%)의 높은 사망률

- 국내의 경우 2000-2010년 입원한 환자들을 대상으로 한 다기관 연구에서 21.2%(21/99)의 환자가 입원 치료 중 사망, 최근(2012-2015년) 시행된 연구에서도23.2%(39/168)의 환자가 사망

Pathophysiology

- Deep fascial layer에 infective process (anaerobe)
  - Phlegmon(abscess) with edema and necrosis
- Blood supply to skin is affected
  - Skin: Perfusion pressure ↓, ischemia ↑

  → Rapid progression of Infection

  (hypoxia induced PML dysfunction)
- Local hypoxia with Up-regulation of endothelial adherence molecule

  : leukocyte adhesion, endothelial cytotoxicity
- Tissue necrosis, purulent discharge, gas production

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CLASSIFICATION

It is difficult to classify…

- Assumed causative microorganism
- Involved tissue
- Required therapy
- Rate of progression
- Initial clinical findings

Amsterdam classification

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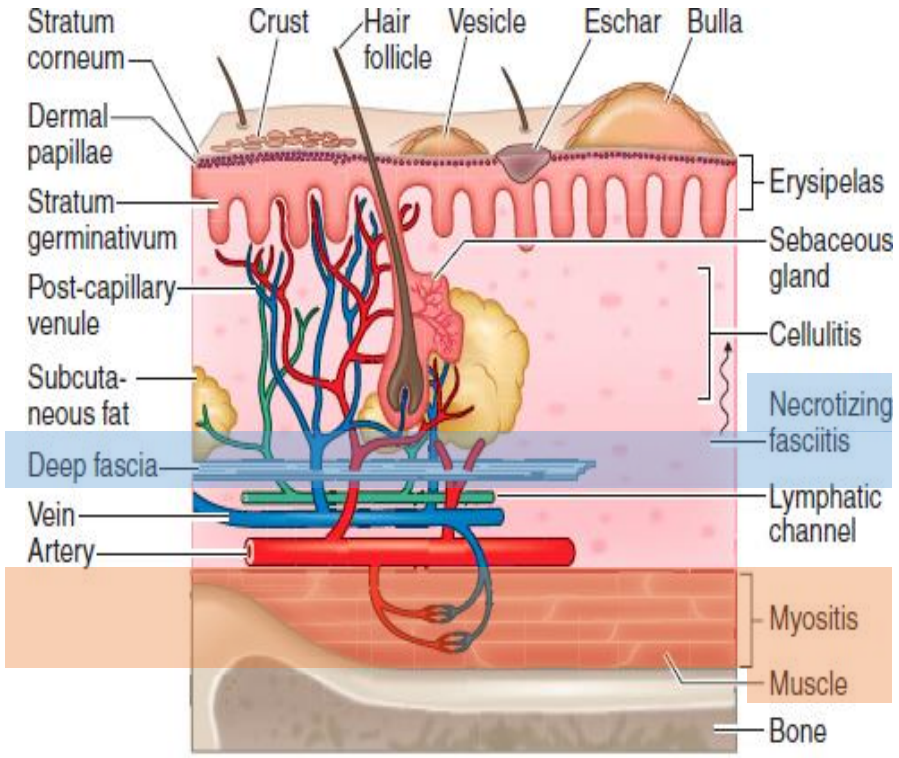
Amsterdam classification

- Progressive bacterial gangrene
  - Anaerobic
    - Clostridial
    - Nonclostridial
  - Aerobic
  - Mixed
- Necrotizing fasciitis
  - Anaerobic
  - Aerobic
  - Mixed
- Myositis and myonecrosis
  - Anaerobic
    - Clostridial
    - Nonclostridial (streptococcal)
  - Others
    - Aerobes
    - Viruses
    - Parasites



Source: J.L. Jameson, A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo, J. Loscalzo: Harrison's Principles of Internal Medicine, 20th Edition
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- Simple model – necrotizing fasciitis vs. nonnecrotizing ST infection At admission
  - ✓ WBC > 15,400
  - ✓ Na^+ < 135 mmol/L

Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score.

Variable, Units	Points
C-Reactive Protein, mg/L	
< 150	0
≥ 150	4
Total white cell count, x $10^3/\mu L$	
< 15	0
15–25	1
> 25	2
Hemoglobin, g/dL	
> 13.5	0
11–13.5	1
< 11	2
Sodium, mEq/L	
≥ 135	0
< 135	2
Creatinine, mg/dL	
≤ 1.6	0
> 1.6	2
Glucose, mg/dL	
≤ 180	0
> 180	1

Modified from Wong et al [8]

The maximum score is 13; a score of ≥ 6 should raise the suspicion of necrotizing fasciitis and a score of ≥ 8 is strongly predictive of this disease.

- A total score of 8 or more is strongly predictive of an NSTI.

Surgical therapy

- Gram
  "closed infection" needle aspiration → more reliable

- Sonography / CT / MRI : to clarify involved anatomic site

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Progressive Bacterial Gangrene

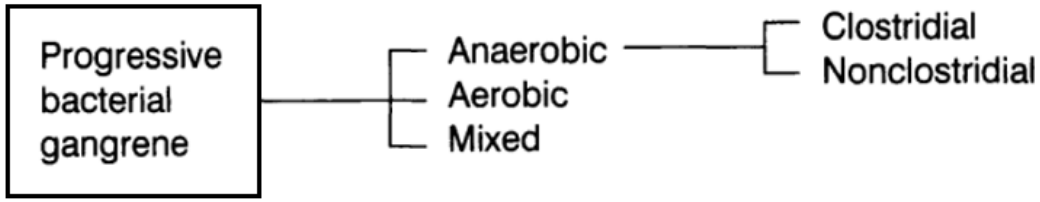
Postoperative progressive bacterial synergistic gangrene
Cullen's ulcer
chronic infectious skin gangrene

- anaerobic crepitant / clostridial cellulitis
- pyoderma gangrenosum
- erysipelas
- gangrenous / necrotizing erysipelas
- symbiotic gangrene
- phagedena geometrica

- directly related to skin infection
- epidermis, dermis, SQ tissue, lymphatics, hair follicle, ~~deep fascia~~

~~muscle compartment~~

- group A streptococci, *S. aureus*
- anaerobic microorganism : *Bacteroides* spp., *Clostridium* spp., Enterobacteriaceae, *Proteus*, *Pseudomonas*...



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Progressive Bacterial Gangrene

- **Always, Very painful!**

- Infection → marginal cellulitis → centrifugal necrosis skin SQ
  patchy, purplish discoloration

- Extensive ST damage, vascular insufficiency
  → true <u>clostridial</u> <u>myositis / myonecrosis</u>

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Necrotizing Fasciitis

hemolytic streptococcal gangrene
Meleney's ulcer
acute dermal gangrene

- Hospital gangrene
- Suppurative fasciitis
- Fournier's gangrene
- Synergistic necrotizing cellulitis
- Hemolytic streptococcal gangrene

- **Deep fascia → SQ tissue, skin**
- **rapidly spreading along deep fascial plane**
  More extended than visible change

- **Fade-out margin : pathognomonic feature**
- **Surgical wound, injured site, spontaneously**

Necrotizing fasciitis
- Anaerobic
- Aerobic
- Mixed

✓ *Streptococcus pyogenes*

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Nonclostridial Myonecrosis

- vs. Gas gangrene?

  - Greenish necrotic muscle
    cf. gas gangrene(clostridial myonecrosis): black necrotic muscle
  - More inflamed appearance than gas gangrene
  - Less gas amount

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THERAPY

- Surgical debridement
- Appropriate antibiotics
- Nutritional support
- Optimal oxygenation – HBO_2

Necrotizing fasciitis HBO_2 positive report

- Necrotizing fasciitis
  - Wilkinson and Doolette *(2004 Arch surg)*
    - Retrospective cohort study, 44 patients
    - HBO_2 increased survival (odd ratio 8.9)
  - Devaney *(2015 Anaesth Intensive Care)*
    - 341 pts, retrospective case controlled study, 275명 HBO_2시행
    - Mortality: HBOT group 12 % Vs. non-HBOT group 24.3%
- Fourniere's gangrene
  - Hollabaugh, retrospective 26 cases *(1998 Plast Reconstr Surg)*
  - Mortality: HBOT group 7% Vs. non-HBOT group 42 %(p=0.04)

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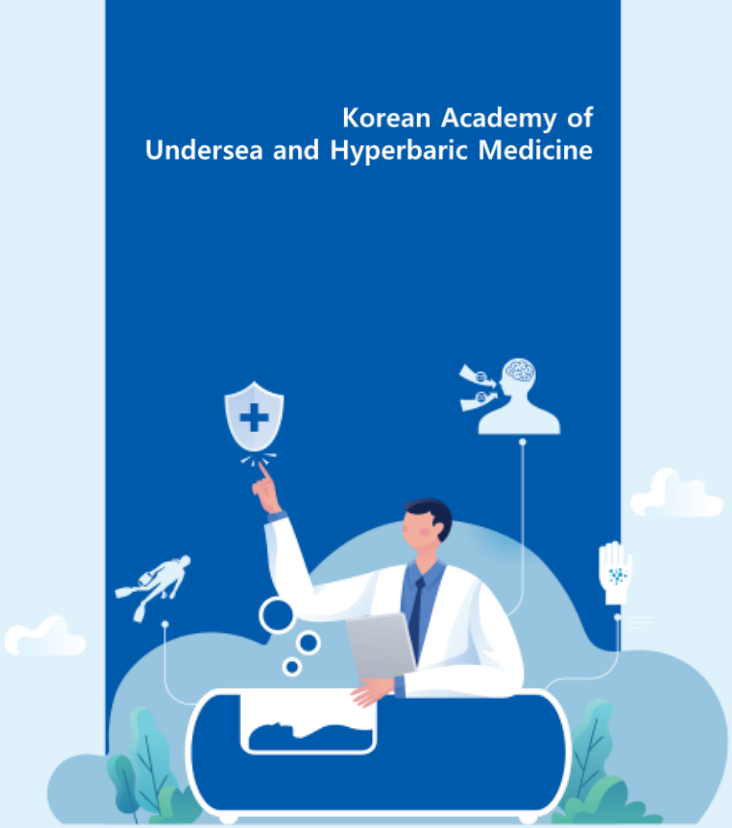
Clostridial myonecrosis (gas gangrene)

- 3 ATA (90 min)
- 1st day：three times
- Twice per day (2~5days)

Ⅳ 요 약



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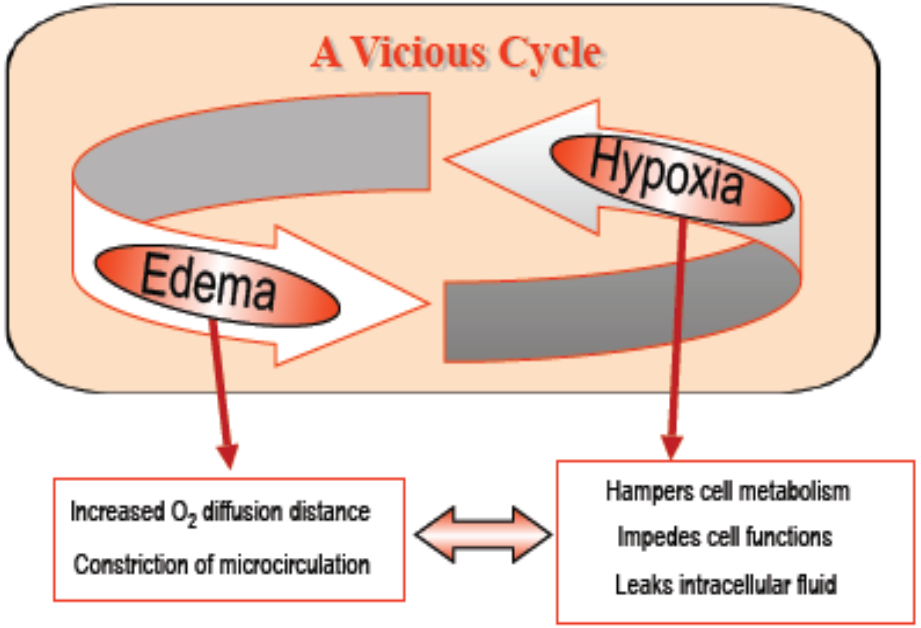
Acute wound


A Vicious Cycle
Hypoxia
Edema
Increased O_2 diffusion distance
Constriction of microcirculation
Hampers cell metabolism
Impedes cell functions
Leaks intracellular fluid

Wound Healing

- Control contamination/infection
- Resolution of inflammation
- Regeneration of connective tissue
- Neovascularization
- Wound contraction
- Resurfacing

Depend on

* **perfusion**
* **oxygen availability**

- Although RCT's do not exist, the mechanism of HBO make sense in mitigating(완화) the pathophysiology of these conditions

□ HBO_2 is always an adjunct to antibiotics and surgery

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Thank you

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