Physiological and Pharmacological Basis of Hyperbaric Oxygen Therapy

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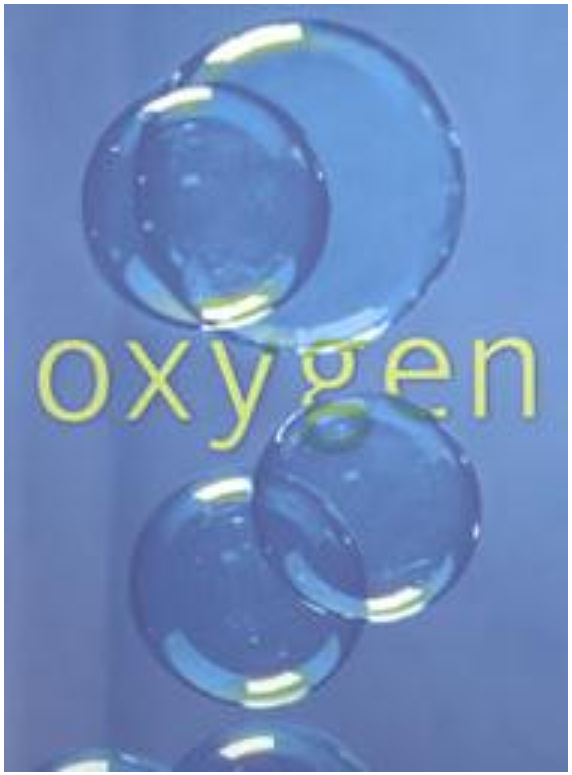
Objectives

- Knowledge of the physiological and pharmacological basis of HBOT in its clinical applications.
- Knowledge of the dangers of oxygen toxicity associated with HBOT treatment

Scope

- What is Hyperbaric Oxygen Therapy (HBOT)?
- Basis of HBOT
  - Physiological basis for HBOT
  - Pharmacological basis for HBOT
- How is HBOT administered?



What is Hyperbaric Oxygen Therapy?

- Treatment in which the patient breathes 100% oxygen intermittently while inside a treatment chamber at a pressure higher than sea level pressure (i.e. > 1ATA)
- Patients can breathe in 100% oxygen by wearing a transparent hood or a mask
- Primary treatment modality in certain conditions; typically used as an adjunct to surgical or pharmacologic interventions in other conditions

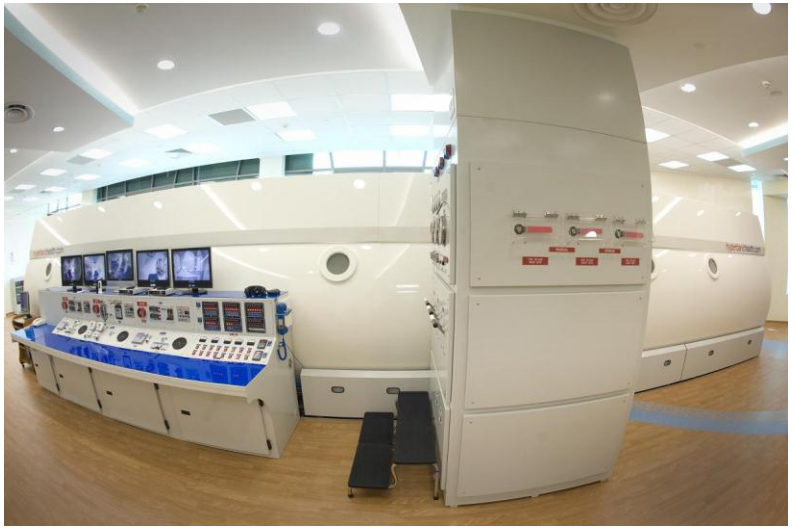
What is Hyperbaric Oxygen Therapy?

- Patient must receive the oxygen by inhalation within a pressurized chamber
- Treatment can be carried out in either a mono- or multiplace chamber and chamber pressurised above sea level pressure (generally > 1.4ATA or higher)
- Breathing 100% O_2 at 1ATA or exposing isolated parts of the body to 100% O_2 (even if pressurised) does not constitute HBOT

Typical Monoplace Chamber

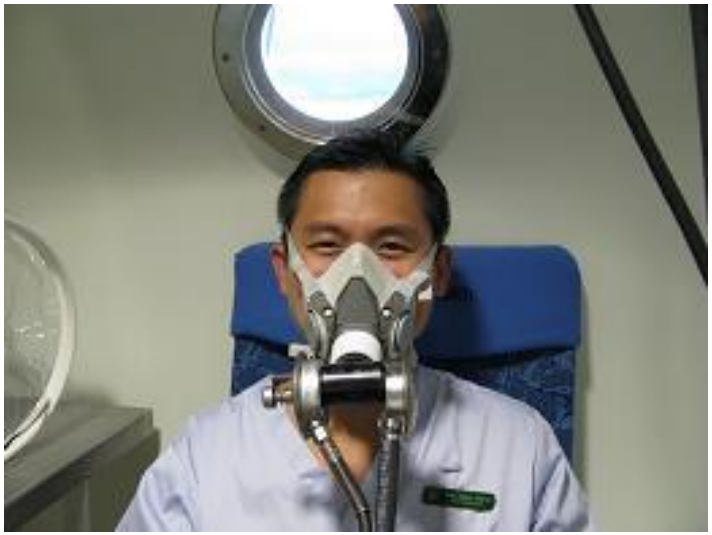
Dual Place Chamber

SGH Multiplace Chamber



Oxygen Delivery Systems

Amron Hood



Scott's BIB

Free flow mask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Physiological Basis for HBOT

- Physical laws for gases
  - Boyle's Law : P1/P2 = V2/V1
  - Dalton's Law : $P_{total}=PO_2 + PN_2 + P_{others}$
  - Henry's Law : P1/P2 = A1/A2
  - Law of Gaseous Diffusion
- Behaviour of gases under different pressures gives rise to many of the physiological effects of HBOT

Physiological Basis for HBOT

- Gas Volume Effects
  - Volume of gas in body tissues and enclosed body areas respond to surrounding pressure changes in accordance to Boyle's Law
  - Bubble volume decreases by half when surrounding pressures are doubled
  - Relief of vascular obstruction by bubbles; less tissue distension when bubbles contract; improve capillary perfusion

Physiological Basis for HBOT

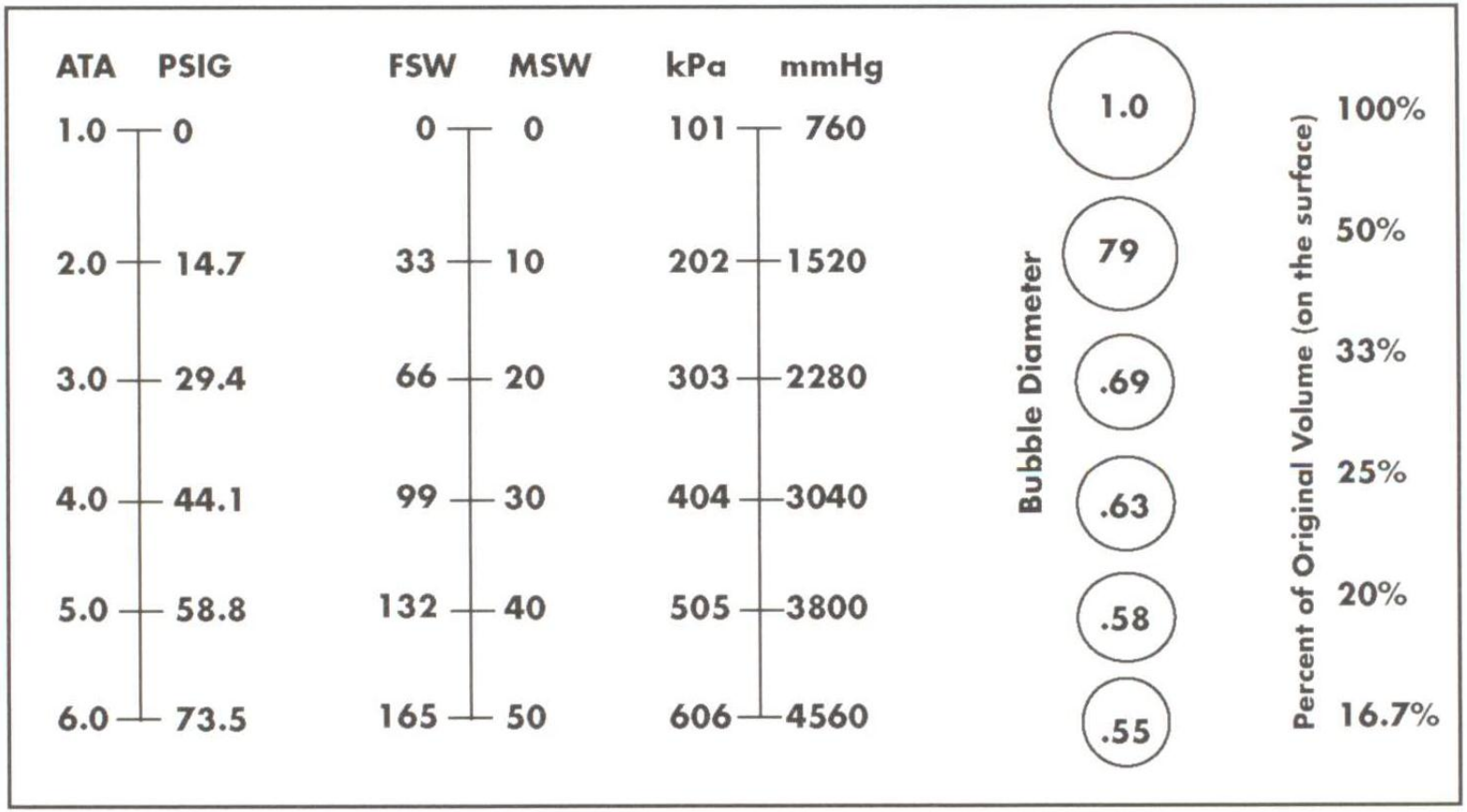


Figure 1. Bubble Volume and Diameter Versus Total Pressure Applied

Physiological Basis for HBOT

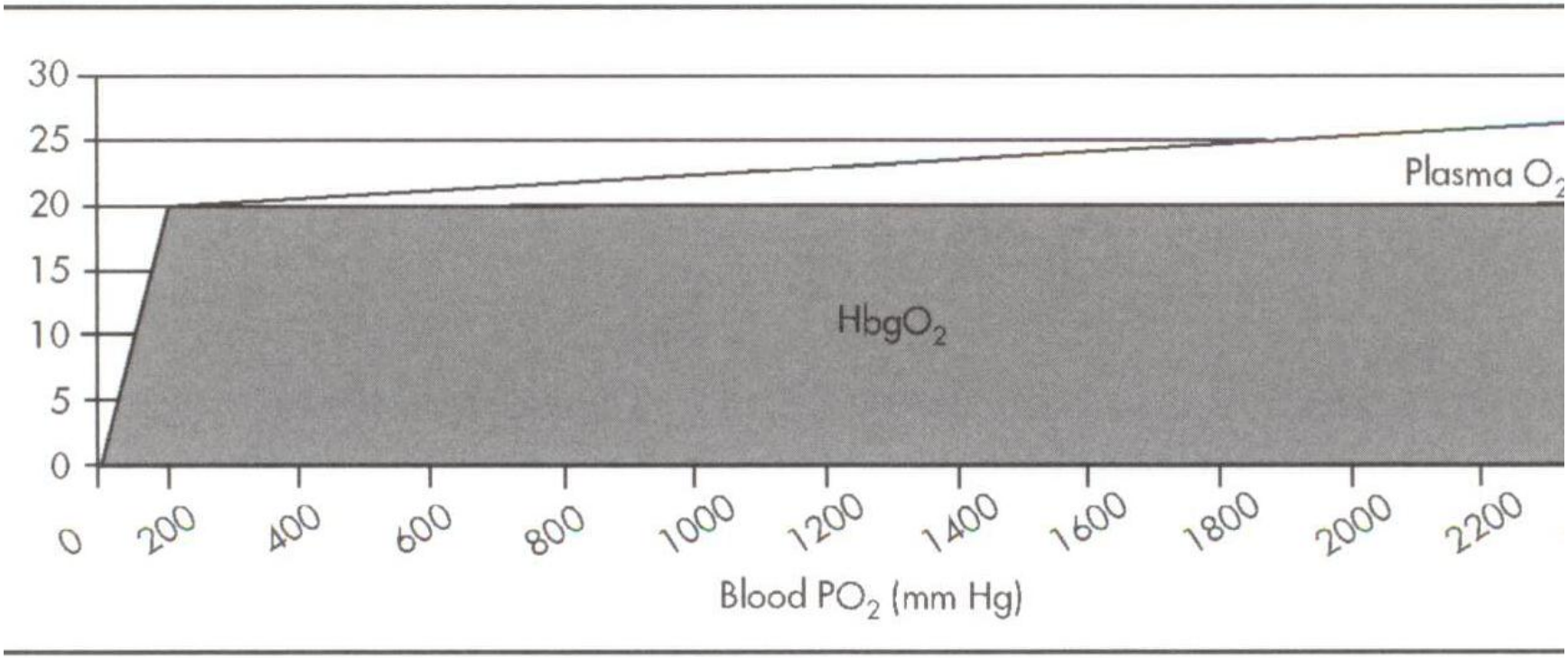
- Increased dissolved O_2 content in plasma
  - ~0.3ml per dl whole blood at sea level pressure
  - ~2.1ml per dl if breathing 100% O_2 at sea level
  - ~4.4ml per dl if breathing 100% O_2 at 2 ATA
  - ~6.8ml per dl if breathing 100% O_2 at 3 ATA
  - mean tissue extraction ~6ml of O2 per dl of circulating blood;
  - Sufficient dissolved O_2 if breathing 100% at 2.8 ATA to meet tissue's basal metabolic requirements

Plasma Oxygen Content

TABLE 1. OXYGEN VALUES ENCOUNTERED DURING HBO THERAPY

In The Breathing Media			In The Lung	In The Plasma
Total Pressure (ata)	Total Pressure (mm Hg)	PO_2 (mm Hg)	PAO_2 (mm Hg)	ml O_2/dl whole blood (vol%)
Breathing Air				
1	760	160	100	0.31
2	1520	319	269	0.83
2.36	1794	377	322	1.00
2.82	2143	450	400	1.24
3	2280	479	429	1.33
4	3040	638	588	1.82
5	3800	798	748	2.32
6	4560	958	908	2.81
Breathing 100% Oxygen				
1	760	760	673	2.08
2	1520	1520	1433	4.44
2.36	1794	1794	1707	5.29
2.82	2143	2143	2056	5.80
3	2280	2280	2193	6.80
4	3040	To minimize risk of oxygen toxicity, 100% oxygen is not used at pressures greater than 3 ata (3.03 MPa)		
5	3800			
6	4560			

Oxygen Content in whole blood



3. Combined Blood Oxygen Content Bound to Hemoglobin and Dissolv
a at High Levels of Blood PO_2 (2)

Physiological Basis for HBOT

- Improved Gas exchange between blood & tissues
  - Higher arterial oxygen tension = larger gradient facilitates oxygen diffusion between functioning capillaries & tissues
- Improved oxygen diffusion limits
  - Arterial PO_2 >2000mm Hg achieved with 100% O_2 at 3 ATA c.f. 100mm Hg with air at sea level
  - 20-fold increase in PO_2 can cause O_2 diffusion distance to increase 4-fold

Enhanced Gaseous Diffusion

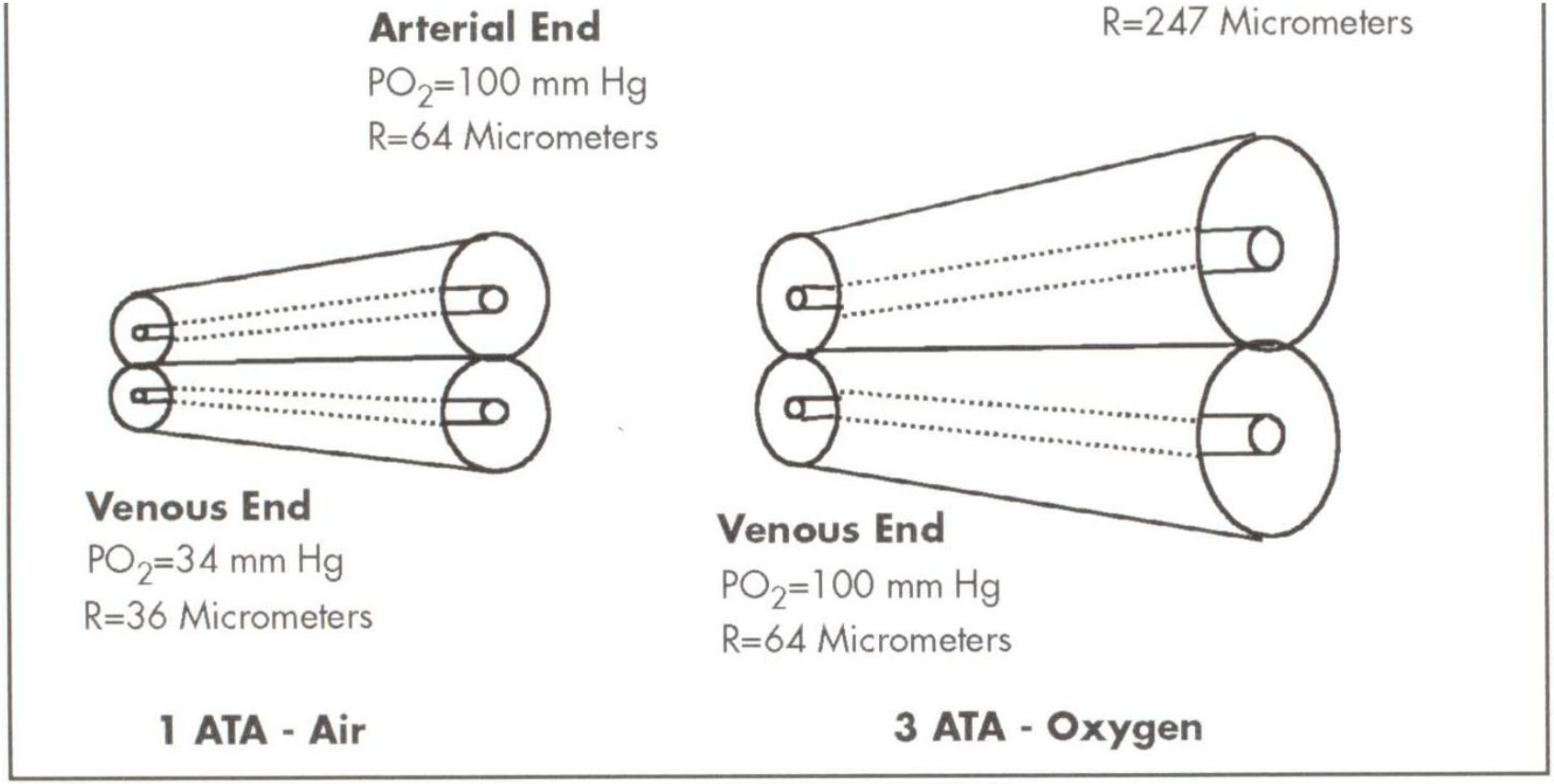


Figure 7.

Pharmacological Basis for HBOT

- Oxygen as a therapeutic drug
  - Minimum Effective Concentration
  - Minimum Toxic Concentration (O_2 toxicity effects)
- Therapeutic window for Oxygen dependent on:
  - Concentration of inspired O2 (FiO_2)
  - Ambient pressure (PO_2)
  - Duration

Antibacterial Effects of HBO

- Enhanced mobility and bacteria killing ability of leukocyte
- Enhance oxidative killing by neutrophils (enhanced generation of reactive oxygen species)
- Directly inhibits production of clostridial alpha-toxin, which destroys cell membranes and increases cell permeability
- Augments action of certain antibiotics, e.g. aminoglycosides, vancomycin

HBO Improves Wound Healing

- Modifies a variety of growth factor and cytokine effects
  - HBO induces production of Vascular Endothelial Growth Factor (VEGF)
    - Stimulates capillary budding, arborization, and granulation formation within wound bed
  - Stimulates Platelet-derived Growth Factor
  - Synergistic effect with Basic Fibroblast Growth Factor

HBO Improves Wound Healing

- Preservation of epidermal basal membrane (in burns)
- Significantly less leukocyte infiltration (anti-inflammatory effects)
- Increase in availability of ATP in tissue
- Reduced edema

1. Hammarlund et al. Hyperbaric oxygen reduced size of chronic leg ulcers: a radnomised double-blind study. Plastic. Reconstr Surg.1994;93(4):829-33
2. Niezgoda et al. The effect of hyperbaric oxygen therapy on a burn wound model in human volunteers. Plast. Reconstr. Surg.1997 May.99:1620-1625

HBO promotes Neovascularization

- Fibroblasts synthesize collagen with oxygen which is required for cross linking of the collagen
- Increased synthesis of hyaluronic acid and proteoglycans by fibroblasts
- Acceleration of angiogenesis (with increase in endothelial cell proliferation)

Tompach et al. Cell response to hyperaric oxygen Treatment. Int.J. Oral Maxillofac. Surg. 1997;26:82-86

HBO promotes Neovascularization

- Inhibition of leukocyte adherence to injured endothelium (reperfusion injuries)
- Enhances recovery of blood flow
- Enhances functional capillary density

Bouachour et al. Hyperbaric oxygen therapy in the management of crush injuries: a randomised double-blind placebo-controlled clinical trial. J Trauma. 1996;41:333-339

HBO promotes Neovascularization

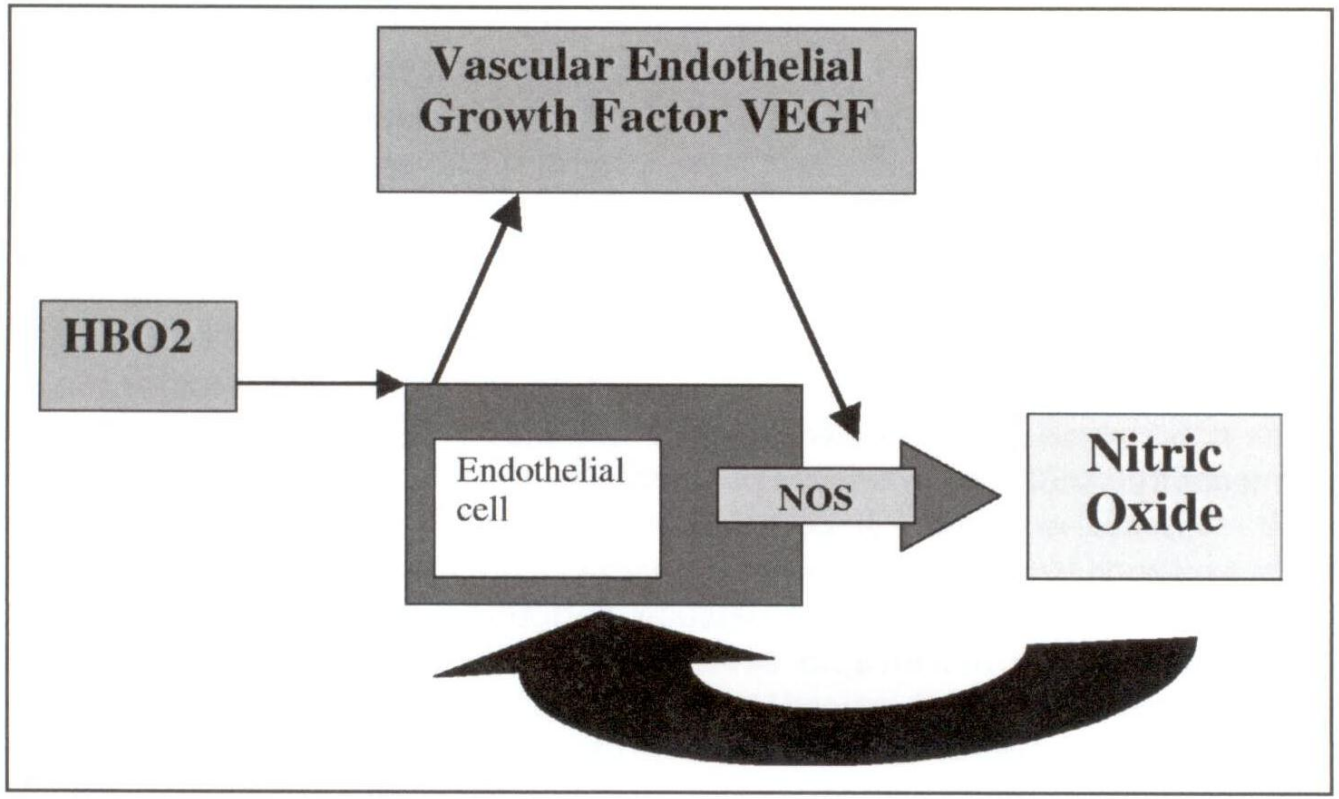


Figure 15. HBO and Vascular Growth

HBO potentiates vascular growth by stimulating the synthesis of NO.

HBO effects on cerebral vasculature

- Mediates vasoconstriction/decreases CBF but increases cerebral oxygen content
- Induces a cerebral ischaemic tolerance
- Net reduction in cerebral oedema
- Affects CNS response to haemodilution
  - CBF normalizes more rapidly when HBO administered during hemorrhagic resuscitation

Other Pharmacological effects

- HBO Modulates Nitric Oxide (NO) production
  - Effects on vasculature – reduction in blood flow in hyperoxic tissues but no reduction in hypoxic tissues
  - Oxidant production applicable to infection control, proliferation, VEGF, collagen synthesis, protein synthesis
  - NO contributes to host defence against pathogens
- Prevents lipid peroxidation (main causes of tissue injury)

Other Pharmacological effects

- Preventive effect against delayed neuronal death
  - Inhibition of NO synthase prevents glutamate neurotoxicity

Summary of beneficial effects of HBOT

- Primary effect
  - Hyperoxygenation – increase diffusion distance
  - Direct pressure - bubble size reduction
- Secondary effects
  - Neovascularisation – new blood vessel formation
  - Fibroblast proliferation – new cell formation
  - Leukocyte oxidative killing – improved infection control
  - Toxin production inhibition/inactivation
  - Vasoconstriction – reduce oedema
  - Reduce harmful effects of reperfusion injury
  - Antibiotic synergism – improve infection control

Summary

Questions?