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Hyperbaric Oxygen Therapy

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Hyperbaric oxygen therapy has been accepted and also recommended in a wide variety of medical conditions. In the last 50 years there have been several studies clarifying the mechanisms of action in the use of hyperbaric oxygen therapy. However, despite the substantial evidence that hyperbaric oxygen has a therapeutic effect in certain carefully defined diseases, many practitioners remain unaware of these findings. This review clarifies the indications currently considered appropriate for hyperbaric oxygen and briefly explains the mechanism of action and its potential use. Evidence shows that hyperbaric oxygen therapy is the main treatment in decompression sickness, arterial gas embolism, severe carbon monoxide poisoning and smoke inhalation, prevention and treatment of osteoradionecrosis, refractory osteomyelitis, radiation induced injury, acute traumatic ischemic injury, exceptional anemia, diabetic foot, venous and arterial ulcers, skin graft and flap healing, central retinal artery occlusion and others. The use of hyperbaric oxygen therapy is expanding.

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Hyperbaric oxygen therapy is applying 100% oxygen under pressure in excesses of two atmospheric or more in a chamber. Hyperbaric oxygen therapy has been a focal interest of many physicians, whichcontributed to the understanding of this modality of treatment.Evidence based data was published about the mechanisms of action and the effect of hyperbaric oxygen therapy treatment on the human body. Although there is a substantial evidence which supports the hyperbaric oxygen therapy, many physicians remain unaware of these findings.

The aim of this review is to introduce this treatment modality and to improve the patients' and physicians' knowledge of hyperbaric oxygen therapy as an adjuvant therapy for healing.

History of Hyperbaric Oxygen Therapy

The variation in the atmospheric changes was first documented more than 300 years ago.In 1664 Henshaw wrote that he treated acute and chronic diseases of all kinds by the modification of atmospheric pressure[1]. In the 1870 Fontaine built an early chamber which was used as the first hyperbaric operating room, see figure 1[2].

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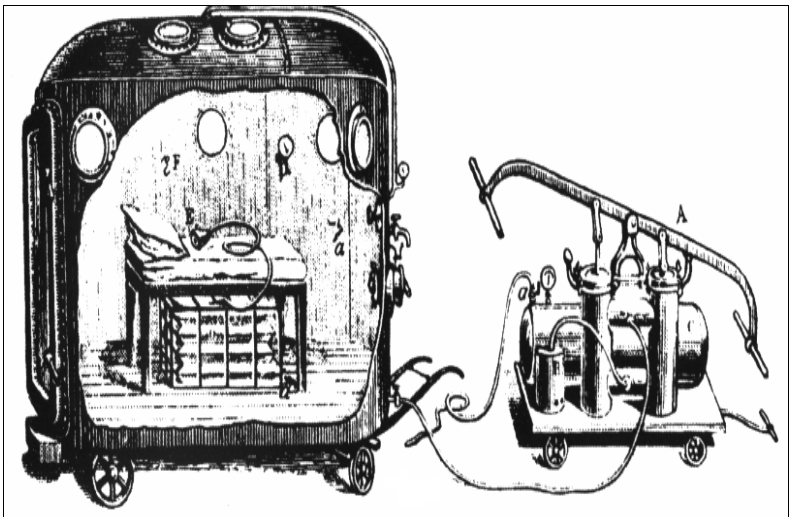

Figure 1: Fonteine's Hyperbaric Operating Room

Some pioneer surgeons, at that time, performed operations within hyperbaric chambers and reported favorable results[3].Paul Bert described that breathing oxygen under pressure can cause a grand mal seizure andaffectthe central nervous system[4]. Lorraine-Smith wrote that 73% oxygen at 1 atmospheric absolute(ATA)pressure causes fatal pneumonia in rats[4,5].Boerema and Churchill-Davidson implemented the use of hyperbaric oxygen therapy[3,5,6]. There was a concern by many hyperbaric physicians that HBO was used indiscriminately; this led to the establishment of the Hyperbaric Oxygen Therapy Committee of the Undersea Medical Society (UMS). They became internationally recognized authority on accepted indications for hyperbaric oxygen therapy. Now, the committee is known asUHMS (Undersea and HyperbaricMedical Society).Table 1 provides a list of indications recommended by the European committee of hyperbaric Medicine (ECHM)[7].

Table 1: Accepted Indications for HBO Therapy[7]

Condition	**Accepted**		
Level of Evidence	**A***	**B***	**C***
Type I			
CO Poisoning		X	
Crush syndrome		X	
Osteoradionecrosis after dental extraction		X	
Osteoradionecrosis (mandible)		X	
Soft tissue radionecrosis (cystitis)		X	
Decompression accident			X
Gas embolism			X
Anaerobic or mixed bacterial anaerobic infections			X
Type II			
Diabetic foot lesion		X	
Compressed skin graft and musculocutaneous flap			X
Osteoradionecrosis (other bones)			X
Radio-induced proctitis/enteritis			X

Radio-induced lesions of soft tissues	X
Surgery and implant in irradiated tissue (prophylaxis)	X
Sudden deafness	X
Ischemic ulcer	X
Refractory chronic osteomyelitis	X
Neuroblastoma Stage IV	X
Type III	
Post anoxic encephalopathy	X
Larynx radionecrosis	X
Radio-induced CNS lesions	X
Post-vascular procedure reperfusion syndrome	X
Limb reimplantation	X
Burns > 20% of surface area and 2nd degree	X
Acute ischemic ophthalmological disorders	X
Selected non-healing wounds secondary to inflammatory processes	X
Pneumatosis cystoids intestinalis	X

*A: Recommendation supported by level 1 evidence (at least 2 concordant, large, double-blind, controlled, randomized studies with little or no methodological bias). *B: Recommendation supported by level 2 evidence (double-blind controlled, randomized studies but with methodological flaws; studies with only small samples, or only a single study). *C: Recommendation supported only by level 3 evidence (consensus opinion of experts).

Types of Hyperbaric Chambers

1. Multi-Place chamber accommodates more than two patients at a time and could be manufactured to any standers and number of occupants, see figure 2.

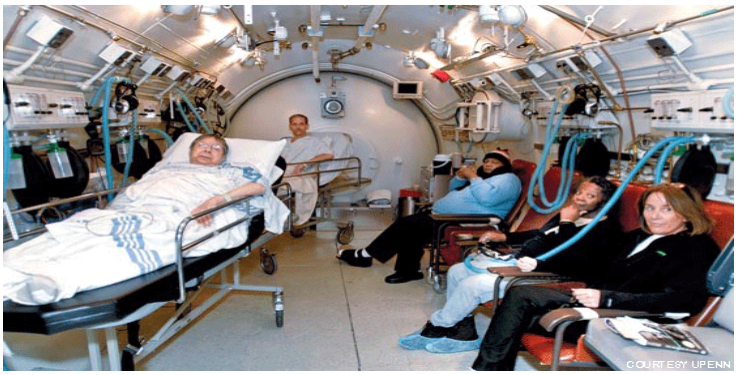

Figure 2: Multi-Place Chamber

2. Mono-Place Chamberaccommodates a single patient only; it is light, portable and could be fixed and operated at any medical facility, see figure 3.

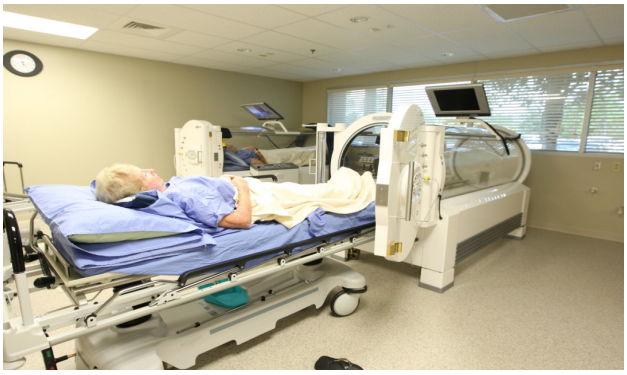

Figure 3: Mono-Place Chamber

Mechanisms of Action of HBO

There are several mechanisms that are associated with hyperbaric oxygen therapy.

Hyperoxygenation

Hyperbaric oxygen exerts its effects by elevation of the inspired gas together with an increased proportion of inspired oxygen.

By breathing air at sea level 1 ATA, 0.32mL of $O_2$is dissolved in 100deciliter of plasma, by increasing the pressure to 3 ATA (60 feet) this will increase O_2 up to 6.8mL/100deciliterin the plasma, approximately 10 folds as verified by Boerema in the "life without blood", see figure 4[8].

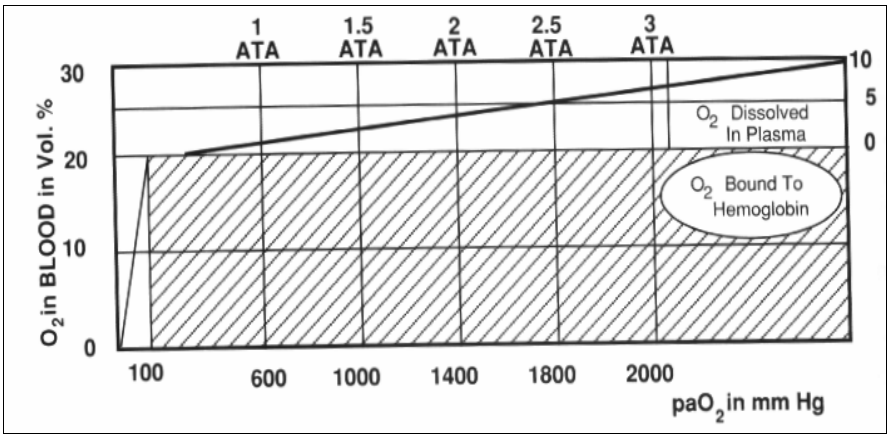

Figure 4:Dissolved Oxygen in the Plasma at Increasing Atmospheric Pressure

In resting humans, the arteriovenous O_2 difference is approximately 5-6% volumes. That amount of oxygen is necessary to sustain human life. This quantity of dissolved oxygen is present in solution at 3 ATA (approximately 6.6 volume % of oxygen dissolved in plasma). Roughly speaking, every increase of 100 mmHg adds about 0.3% volume of dissolved oxygen in blood, see table 2.

Table 2: ArterialOxygen Tension and Oxygen Blood Content in Different Depth[9]

Inhaled Oxygen Fraction	Absolute Pressure	Arterial Oxygen Tension (mmhg)	Oxygen in Plasma (Ml Per Dl of Blood)
0.21	(1 ATA)	100	0.31
1.0	(1 ATA)	660	2.0
1.0	(2 ATA)	1400	4.3
1.0	(3 ATA)	2200	6.8

Vasoconstriction

Exposure to oxygen at pressure results in 20% reduction in blood flow in normaltissues (vasoconstriction). This effect is offset by the tenfold increase inthe oxygen content of plasma[10]. The vasoconstrictive action is useful in the treatment of diabetic foot, crush injuries, acute thermal burns and cerebral edema. Because the diffusion of oxygen through plasma is proportional to the square root of the distance from the capillary to the cell, even small reductions in edema result in significantly more oxygen reaching the cell[11].

Fibroblast Proliferation and Collagen Deposition (Neovascularization)

At tissue oxygen tensions less than 10-15 mmHg, fibroblast loses the ability to synthesize collagen, migrate or divide. In hypoxic bone, new bone formation cannot take place following injury. The administration of hyperbaric oxygen allows fibroblasts to synthesize collagen; osteoclasts to deposit bone; therefore, rapid wound healing[12,13].

Hyperbaric Oxygen Effect on Microorganisms and Host Immune Response

Hyperbaric oxygen therapy was found to be bactericidal;O_2therapy enhances the ability of white blood cells to destroy bacteria. Pressure of oxygen above 4 mmHg is lethal for strict anaerobes.HBO has bacteriostatic and even bactericidal effects on *Clostridia*, E. coli, as well as on many Enterobacteria, Pseudomonas aeruginosa and Enterococcus faecali[14-16]. The inhibiting or lethal effect of oxygen varies with the strain of Clostridium bacteria reproductive cycle in different pressure of oxygen exposure[17]. HBO enhancesantibioticactivity;several studies have provedthat increased tissue oxygentension reduces the minimum inhibitory concentrations and the minimum bactericidalconcentration of E. Coli, Enterobacter, Klebsiella, and Staphylococcus againstdifferent aminoglycosides[16,18].Combining HBO with antibiotics and surgery would be an adjunctive therapy for treating tissue infected by both anaerobic and aerobic bacteria in hypoxic wounds and tissues[19].

Reduction in Bubble Size

Decompression sickness and gas embolism both involve the presence of gas bubbles within the bloodstream or tissues[20]. The quickest way to reduce the size of such bubbles and allow for the rapid relief of symptoms is compression within hyperbaric chamber. In addition, if the patient is breathing 100% oxygen, nitrogen exits from the bubble even faster. This is because after equilibrium the bubble still contains about 80% nitrogen while the surrounding blood has none. This steep diffusion gradient allows nitrogen to leave the bubble at a rate greater than would

occur if only compressed air was being breathed. This is the principle of counter diffusion[21]. Increasing the ambient pressure from 3 to 6 ATA results in less dramatic reductions in bubble size, but may result in a greater incidence of oxygen toxicity.

Contraindications

The patient's underlying conditions should guide the physician in deciding whether the benefit from HBO therapy outweighs the potential harm. Contraindications to HBO exist and are classified as being either absolute or relative. These apply to patients as well as to medical personnel who enter the multi-place chamber.

Absolute Contraindications

1. Untreated Pneumothorax

The patient who has been compressed to a given depth, the pressure within his pleural cavity comes into equilibrium with the pressure within the chamber. The danger occurs during the subsequent decompression phase. For example, decreasing the ambient pressure from 3 ATA to 1 ATA triples the volume of air trapped within the pneumothorax, this could lead to a tension pneumothorax[22].

2. Drug Interaction: Anti-cancer Drugs (Cisplatinum, Doxorubicin, Bleomycin)

Chemotherapy is toxic to the cells, rapidly dividing or metabolically active cells are affected most. Chemotherapy and HBO could cause extreme toxicity and is contra-indicated. Bleomycin toxicity may be life-long, after a course of therapy; patients receiving HBO after completion of chemotherapy should be carefully examined for signs of pulmonary fibrosis. Adriamycin and Cisplatinum therapy poses no threat 10 days after completion[23].

3. Thoracic Surgery

History of thoracic surgery should alert one to the possibility of air being trappedwithin lung segments.

4. Ear Barotrauma

The ear is prone to develop barotrauma; in some patients this is serious enough to require myringotomy and grommet. When the rate of compression is kept slow, most people can adjust by pinching their nostrils and forcing air into their middle ear spaces (Valsalva or Toynbee maneuvers). Decongestants or antihistamines used before HBO may be helpful in minimizing this problem. History of ear surgery should be sought as HBO may displace or destroy implants. Because the ear is sensitive to the effects of repeated HBO exposure and resulting barotrauma, it is important to be frequently examined. Most clinicians use the Teed's scale in describing their findings.

Teed 0 -Symptoms without signs
Teed 1 - Erythema or injection of the TM, especially along the handle of themalleus
Teed 2 - Erythema or injection plus hemorrhage within the substance of the TM
Teed 3 - Gross hemorrhage within the substance of TM; this appears as bright red patches on the TM
Teed 4 - Deep blue or black appearance of TM indicating free blood filling the middle ear
Teed 5 - Perforation of the TM

If the patient is unable to equalize or has Teed's scale 3 or 4, this would be an absolute contra-indication to HBO.

5. Malignant Disease

Because of theoretical concerns that HBO may enhance tumor growth, this is considered another area of controversy. Controlled animal studies do not support the tumor growth concern, but until further evidence becomes available, HBO should be withheld if active metastatic disease exists. Because increased oxygen levels may worsen endarteritis, patients who have received treatments should wait approximately 6 weeks before the initiation of HBO therapy.

6. Severe Claustrophobia

Many people suffer severe anxiety reaction getting inside the chamber, especially small mono-place chamber. Although this fear might prevent treatment, usually it can be overcome by reassurance or the use of anti-anxiety medications, such as intravenous diazepam. Often, it is useful to show the patient how the actual treatment works and what he expects. Patients should be warned that their voice will alter slightly, so they do not become frightened.

Relative Contraindications

1. Pressure Changes

- **Spontaneous Pneumothorax**

Patients with history of spontaneous pneumothorax or significant amount of chronic obstructive pulmonary disease (COPD) are particularly at risk. Obstruction of bronchioles and distal air trapping produce areas of stress where a pneumothorax could develop. Blebs and bullae are often visible on chest X-ray and could potentially rupture.

- **Asthma or COAD**

Patients having significant amount of chronic obstructive pulmonary disease (COAD) are particularly at risk. Obstruction of bronchioles and distal air trapping produces areas of stress where a pneumothorax could develop.

- **Sinusitis**

Mucus plugging could lead to pain during compression or decompression - a sinus barotrauma. Decongestants or nasal sprays might prevent or minimize these problems.

- **Optic Neuritis**

History of optic neuritis should be ruled out before proceeding with HBO treatment. There have been reports of serious recurrences of optic neuritis, even blindness, following treatment of patients with inactive cases.Patients could develop a squeeze-related injury from air trapped under contact lenses; therefore, they must be removed prior to treatment.

2. Adversely Affected by Increased PO_2

- **Viral Infections**

In patients with pre-existing viral illnesses, there are anecdotal reports of fulminating illness and deaths following HBO treatment. Hart reported the death of 4-year old patient from herpes simplex. Schmidt and Ball have shown that the mortality of animals treated with HBO is quadrupled in the presence of viral disease. Except for life threatening emergencies, many centers recommend the postponement of treatment until the patient has fully recovered. In addition, upper respiratory infection makes it harder for patient to equalize pressure in their ears and sinuses during HBO treatments.

- **Congenital Spherocytosis**

Because of increased red cell fragility, HBO may result in an increased rate of hemolysis.

- **Pregnancy**

The treatment of pregnant patients is controversial. Some studies indicate that no harmful effects were found. The Russian literature states that there is little risk, but Bolton states there is an increased risk of major abnormalities. There are theoretical reasons to be cautious.

3. Increased Risks for O_2 Toxicity

- **Seizure Disorder**

Patients with pre-existing seizure disorders should receive prophylactic anticonvulsant medication before HBO treatments are initiated. Those already receiving such medications should have their serum levels monitored to ensure adequate protection. Some researchers believe Phenobarbital has an advantage over phenytoin in the treatment and prevention of oxygen toxic seizures.

- **Drugs**

Some drugs increase the risk of oxygen induced seizure. Although the exact mechanism is unknown, it is believed they directly or indirectly lower the seizure threshold. Other drugs can cause hypermetabolic states, mild acidosis or CO_2 retention, which predispose to seizures.

CONCLUSION

The use of hyperbaric oxygen therapy as adjuvant therapy is widely used internationally; evidence based literature has proved the effectiveness of HBO in the treatment of wide range diseases. Hyperbaric oxygen therapy is not a new modality of treatment in the world but it has not been implemented in our region.Although HBO therapy is not without side effects,

most specialists in the field consider the risk for patients as acceptable if the condition isclearly indicated.

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Competing interest: None **Sponsorship:** None

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