"When you lose your mind..." Part II: Introduction to Hyperbaric Oxygen Therapy

Dr. C.K. Tam
SMO, Dept. of Rehabilitation & Extended Care
TWGHs Wong Tai Sin Hospital

IHRM

21 August 2008

Why We Need to Know HBOT?

- Request for HBOT by patients and their carers
  - "Expert opinion" from China colleagues
  - Newspaper promotion
  - Public awareness
- Tung Wah Board is planning to set up a hyperbaric chamber
- Availability of home-use HBOT facility
  - Now in HK market

Contents

- Introduction
- How is it done?
- How does it work?
- Indications
- Contraindications
- Side Effects & Safety Issues

What is HBOT?

- HBOT is high dose oxygen inhalation therapy in which a patient breathes pure oxygen while inside a pressurized hyperbaric chamber.
- Undersea & Hyperbaric Medical Society (UHMS) definition: The patient breathes 100% oxygen intermittently while the pressure of the treatment chamber is increased to greater than one atmosphere absolute (ATA).

Background of HBOT

- 1841: 1st caisson for coal excavation.
- 1860-70 Brooklyn Bridge caisson
  - 110 cases of decompression sickness (Caisson disease), 2 fatal.
- 1889: Hudson River Tunnel caisson
  - 1st Recompression chamber on site for treating DCS.
- DCS also found in deep divers since 1930s.

How is it done?

Hyperbaric Chambers

Multiplace Chamber

Monoplace Chamber

Other Hyperbaric Chambers

- Steel Ball Hotel
  - Obsolete.
  - Military purpose.
- Portable Mild Hyperbaric Chamber (1.3ATA)
  - Now available in HK market.
  - Promote as home use.

Multiplace Hyperbaric Chamber

- ≥1 patients can be treated at the same time.
- Min. staffing:
  - 1 operator inside
  - 1 operator outside
  - 1 doctor on site
- Operator inside allow continual medical attendance throughout HBOT.
- O_2 within chamber <23.5%.
- 100% O_2 delivered by hood or mask.
- Fire suppression system required
  - Water pipe, overhead water spray nozzles & deluge from water tank.

Monoplace Hyberbaric Chamber

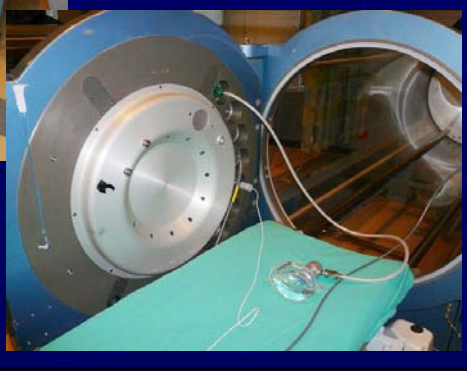
- 1 patient per chamber.
- Commonly 4 chambers per centre.
- Min. staffing:
  - 2 chambers by 1 operator
  - 1 doctor on site
- 100% O2 within chamber.
- Mask for air break.
- No fire suppression system.
- More comfortable, can enjoy audiovisual programs or TV.
- Less space required.

Connections for Patient Monitors

- Continuous monitors when necessary:
  - ECG, BP, TcpO2.
  - Equipment outside chamber.
  - Connection by wires passed through the chamber hull.
  - Equipment may be used inside multiplace chamber if the equipment is tested safe within hyperbaric chamber.
- Blood glucose monitor on DM patients:
  - Pre & post dive check.
  - Blood glucose >6.7mmol/l prior to diving.

Connections for Patient Monitors

Inside

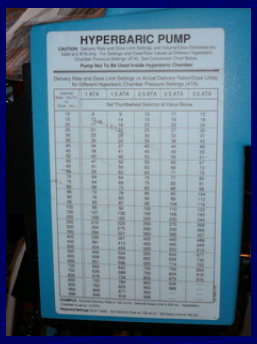


Connections for Patient Monitors

Outside

Connections for Patient Therapy Equipment

1. IV fluid
   - Special pass-through tubing with check valve & locking connectors.
   - Special IV pump with higher force.
   - IV fluid in plastic bags can also be used inside multiplace chamber by gravity or special pump.



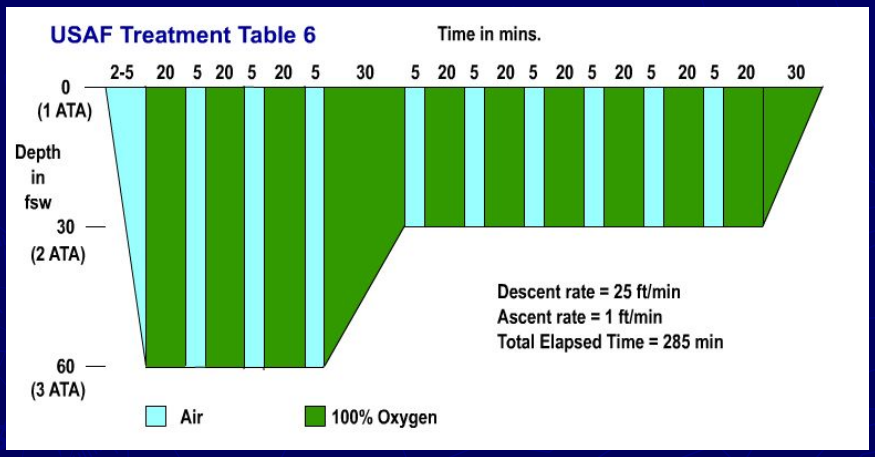
Connections for Patient Therapy Equipment

2. Ventilator
   - Specially designed ventilator for monoplace chamber.
   - Pneumatic ventilator tested safe in hyperbaric chamber can also be used inside multiplace chamber.
   - More commonly use Ambubag inside multiplace chamber during resuscitation.

Connections for Patient Therapy Equipment

3. Tracheostomy tube
   - Deflate cuff and replace air with equal amount of fluid.
4. Suction equipment
   - At depth, suction is created by pressure differential.
   - At surface, vacuum source is required.
5. Drains & Tubes
   - Open system during descent and ascent to avoid fluids back into wound or creating excessive suction.
   - Chest drain must have Heimlich valve.
   - Nasogastric tube – remove plug.
6. Defibrillator
   - Paddles can be wired into a multiplace chamber.
   - Usu. done outside chamber after decompression.

Example of HBOT Schedule (for DCS)



How does it work?

Mechanisms of Action of HBOT

1. Mechanical Effect of Hyperbaric Pressure
   - General Gas Law:

$$PV = nRT$$ or $$\frac{P_1V_1}{T_1} = \frac{P_2V_2}{T_2}$$

Where P=absolute pressure V=volume
n=number of moles R=gas constant
T=absolute temperature

   - Bolye's Law (constant T):

$$P_1V_1 = P_2V_2$$

   - Others: Charles' Law (constant P), Gay-Lussac's Law (constant V)

Mechanisms of Action of HBOT

2. Gas Dissolved in Solution (e.g. plasma)
   - Henry's Law:

$$\frac{P_1}{A_1} = \frac{P_2}{A_2}$$

Where A=amount of gas dissolved in a liquid
P=partial pressure of the dissolved gas

Mechanisms of Action of HBOT

2a) Law of Mass Action (Tx of CO poisoning)

- Affinity of CO to Hb 240x more than O_2.
- Need very high O_2 to displace & eliminate CO.

$$COHb + O_2 \rightarrow HbO_2 + CO$$

	pO_2 (mmHg)
Air	160
100% O_2 at 1 ATA	760
100%O_2 at 3 ATA	2280

Mechanisms of Action of HBOT

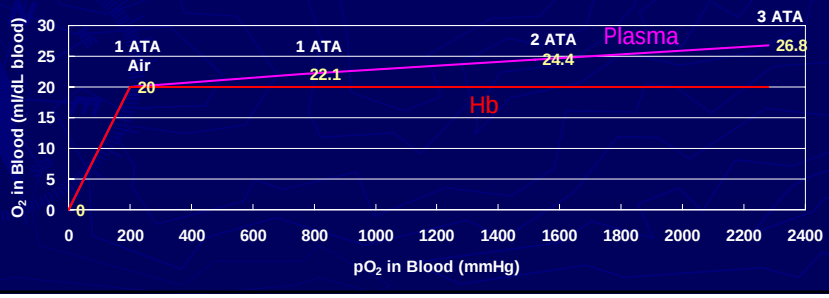
2b) Hyperoxygenation Effect

i) Hemoglobin O_2

- Breathing air at 1 ATA: Hb is 97% saturated, giving 19.8ml O_2/dL blood.
- Breathing 100% O_2: Hb is 100% saturated, little gain.
- HBOT: little benefit.

ii) Plasma O_2

- O_2 solubility is proportional to pO_2 (0.31ml/dL per 100mmHg)

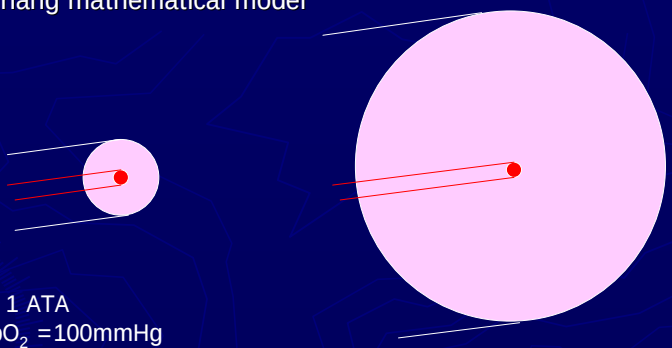


“Life without Blood”

- Prof. Boerema (a cardiac surgeon in University of Amsterdam) present the paper in 1960.
- The first clear demonstration of the ability of HBO at 3 ATA to dissolve sufficient oxygen in the blood to maintain tissue oxygenation, even in the complete absence of circulating functional red blood cells in an experimental pig.
- Initial thoughts of performing cardiac surgery in babies with congenital heart disease within a HBO OT room.

Oxygen Diffusion into Tissues

- Krogh Erlang mathematical model



Air at 1 ATA
Cap pO_2 =100mmHg
Diffusion distance =64 μm

100% O_2 at 3 ATA
Cap pO_2 =2000mmHg
Diffusion distance =247 μm (4x)

- HBOT benefits ischemic & hypoxic wounds by increasing the O_2 diffusion distance, correcting local tissue hypoxia and bringing pO_2 up to normal.

Mechanisms of Action of HBOT

3. Neovasularization
   - As inspired pO_2 increases, tissue pO_2 increases in the skin & wound (Sheffield PJ, Dunn JM, 1979).
   - Multiple HBOT (2 hrs daily) increases resting tissue pO_2 in the wound indicating improved vascularity (Sheffield PJ, Workman WT, 1985).
   - Ischemic & hypoxic wounds become the main bulk of patients for HBOT.

Mechanisms of Action of HBOT

4. Leukocyte Oxidative Killing Effect
   - Increases leukocyte phagocytosis.
   - Improve bacterial killing by neutrophil-generated high energy oxygen radicals.
     - Superoxide dismutase enzyme system protects the patient against high energy O_2 radicals.
   - Effect on Cl. perfringens (gas gangrene):
     - α-toxin release ceases at pO_2 >250mmHg.
     - Bactericidal when pO_2 >1500mmHg.

     (van Unnik, 1965)

Mechanisms of Action of HBOT

5. Other Anti-bacterial Effects
   - Converts anaerobic wounds with low pH to aerobic wounds with normal pH.
   - Some antibiotics do not work well in acid pH.
     - e.g. aminoglycosides, quinolones and certain sulfonamides.
   - Adjunctive HBOT helps control infection.
     - Tobramycin + HBO_2 best eradicates Pseudomonas aeruginosa from infected bone (Mader JT *et al*,1987).

Mechanisms of Action of HBOT

6. Attenuate Reperfusion Injury
   - Direct injury from severe hypoxia.
   - Indirect injury from prolonged ischemia and inappropriate activation of leukocytes during reperfusion.
   - HBO_2 protects tissue from reperfusion injury by:
     - Inhibits sequestrations of neutrophils in venules.

Mechanisms of Action of HBOT

7. Vasoconstriction
   - Hyperoxia causes rapid & significant central & peripheral vasoconstriction.
   - Reduce cerebral edema:
     - Cerebral edema causing secondary brain injury.
     - HBOT reduces cerebral blood flow by 25% while maintaining tissue oxygenation (Sukoff MH, Ragatz RE, 1982).
   - Tx of burns:
     - Reduce tissue edema.
     - Reduce fluid loss.
     - Less scarring.

Indications

Indications for HBOT

125 Indications

1976 Undersea Medical Society - Recommendations made with reference to evidence

12 “Approved” Indications

1996 Undersea & Hyperbaric Medical Society (UHMS)

13 “Approved” Indications

- Both FDA & Health Canada adopt the UHMS recommendation to license use of hyperbaric chambers in their countries.
- Only the 13 Approved indications are covered by insurance.

Indications for HBOT

1. Air or Gas Embolism
2. Decompression Sickness
3. Carbon Monoxide Poisoning ± complicated by Cyanide Poisoning
4. Exceptional Blood Loss (Anemia)
   - For those who cannot be transfused for medical or religious reasons.
5. Clostridal Myositis and Myonecrosis (Gas Gangrene)
6. Necrotizing Soft Tissue Infections
7. Crush Injury, Compartment Syndrome, and other Acute Traumatic Ischemias
8. Osteomyelitis (refractory)
9. Intracranial Abscess
10. Enhancement of Healing in Selected Problem Wounds (e.g. in DM)
11. Delayed Radiation Injury (soft tissue and bony necrosis)
12. Skin Grafts & Flaps (compromised)
13. Thermal Burns (>20% and 2nd degree)

How About Our Cases?

- 1st Case - Exceptional Blood Loss (Anemia)
  - Transfusion of blood products or substitute is mainstay of Tx.
  - HBOT recommended for those who cannot be transfused for medical or religious reasons.
  - No RCT found.
  - HBOT need to be started in the acute stage.
  - ? Role & mechanism of starting HBOT >one year after acute event as in our case.
- 2nd Case - TBI
  - Not an approved indication.

HBOT for TBI

- HBOT has been proposed as a treatment for minimizing secondary brain damage by improving the oxygen supply to the brain.
- Cochrane Review: only 4 RCTs (382 patients) satisfied the inclusion criteria up to 2008.
- Varied methodologies and quality fair to poor.

Study	Method	Patients	Outcomes	Interventions
Artru et al (1976)	RCT, non-blind	Closed HI with coma, mean time from coma to HBOT 4.5 days HBOT: 31 Control: 29	Mortality unfavorable outcome Adverse events	HBOT: 100% O2 2.5 ATA x60min daily x10, repeat 4d later if not regain consciousness or died. Control: not put in chamber
Holbach (1974)	Quasi-RCT, non- blind	Closed HI with coma "acute mid-brain syndrome" HBOT: 49 Control: 50	Mortality Complete recovery	HBOT: 100% O2 1.5 ATA x?min daily x? Control: not put in chamber
Ren (2001)	RCT, non-blind	Closed HI with GCS <9 and stable on D3 HBOT: 35 Control: 20	GCS Favorable GOS	HBOT: 100% O2 2.5 ATA x40-60min 10x over 4 days, repeated if no response. Control: not put in chamber
Rockswold (1992)	Quasi-RCT, assessor blind	Closed HI with GCS <10 and within 6-24hrs HBOT: 84 Control: 84	Favorable GOS (1 or 2) Mortality ICP Adverse events	HBOT: 100% O2 1.5 ATA x60min q8h x2wks or till death or awake. Control: not put in chamber

Mortality at Final FU

Analysis 02.01. Comparison 02 Death at final follow-up, Outcome 01 Death at final follow-up

Review: Hyperbaric oxygen therapy for the adjunctive treatment of traumatic brain injury

Comparison: 02 Death at final follow-up

Outcome: 01 Death at final follow-up

Study	Control n/N	HBOT n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Artru 1976	16/29	15/31		26.6	1.14 [0.70, 1.86]
Holbach 1974	37/50	26/49		48.1	1.39 [1.02, 1.90]
Rockswold 1992	26/82	14/84		25.3	1.90 [1.07, 3.38]
Total (95% CI)	161	164		100.0	1.46 [1.13, 1.87]

Total events: 79 (Control), 55 (HBOT)

Test for heterogeneity chi-square= 1.86 df=2 p=0.39 P =0.0%

Test for overall effect z=2.95 p=0.003

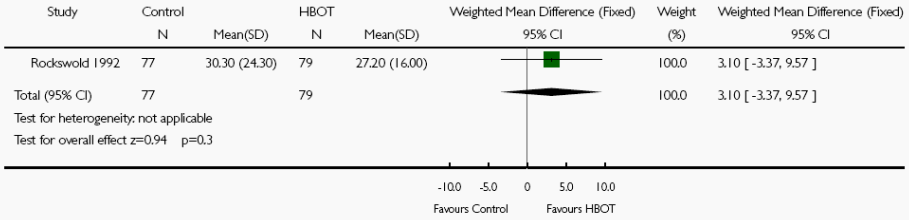
Peak ICP

Analysis 03.01. Comparison 03 Intra-cranial pressure, Outcome 01 Mean peak ICP at any time overall

Review: Hyperbaric oxygen therapy for the adjunctive treatment of traumatic brain injury

Comparison: 03 Intra-cranial pressure

Outcome: 01 Mean peak ICP at any time overall



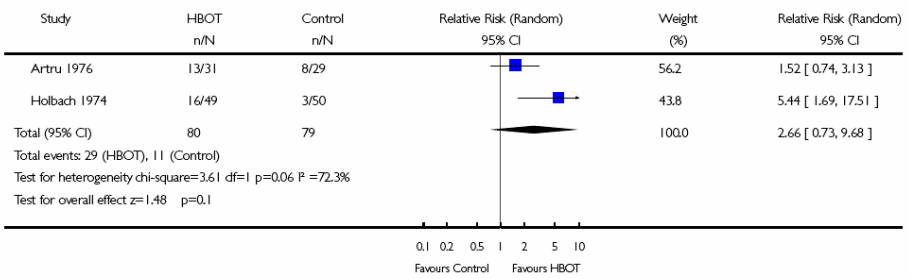
Good Functional Outcome at End of Treatment Period to One Month

Analysis 01.01. Comparison 01 Good functional outcome (GOS <3 or similar), Outcome 01 Good functional outcome at end of treatment period to one month

Review: Hyperbaric oxygen therapy for the adjunctive treatment of traumatic brain injury

Comparison: 01 Good functional outcome (GOS <3 or similar)

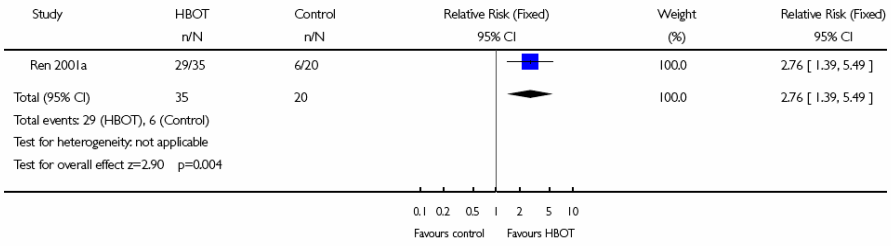
Outcome: 01 Good functional outcome at end of treatment period to one month



Good Functional Outcome at 6 Months

Analysis 01.02. Comparison 01 Good functional outcome (GOS <3 or similar), Outcome 02 Good functional outcome at six months

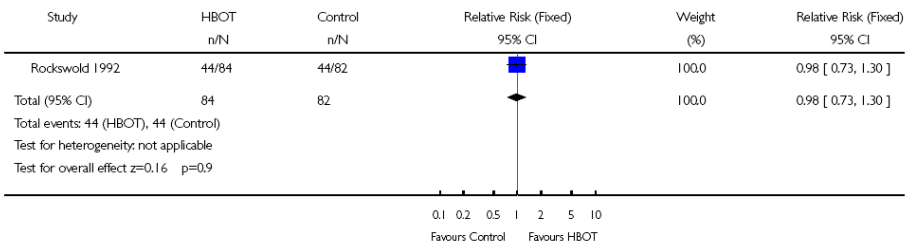
Review: Hyperbaric oxygen therapy for the adjunctive treatment of traumatic brain injury
Comparison: 01 Good functional outcome (GOS <3 or similar)
Outcome: 02 Good functional outcome at six months



Good Functional Outcome at 12 Months

Analysis 01.03. Comparison 01 Good functional outcome (GOS <3 or similar), Outcome 03 Good functional outcome at 12 months

Review: Hyperbaric oxygen therapy for the adjunctive treatment of traumatic brain injury
Comparison: 01 Good functional outcome (GOS <3 or similar)
Outcome: 03 Good functional outcome at 12 months



Good Functional Outcome at Final FU

Analysis 01.06. Comparison 01 Good functional outcome (GOS <3 or similar), Outcome 06 Good functional outcome at final follow-up

Review: Hyperbaric oxygen therapy for the adjunctive treatment of traumatic brain injury

Comparison: 01 Good functional outcome (GOS <3 or similar)

Outcome: 06 Good functional outcome at final follow-up

Study	HBOT n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Artru 1976	13/31	8/29		25.0	1.52 [0.74, 3.13]
Holbach 1974	16/49	3/50		18.1	5.44 [1.69, 17.51]
Ren 2001a	29/35	6/20		25.6	2.76 [1.39, 5.49]
Rockswold 1992	44/84	44/82		31.3	0.98 [0.73, 1.30]
Total (95% CI)	199	181		100.0	1.94 [0.92, 4.08]

Total events: 102 (HBOT), 61 (Control)

Test for heterogeneity chi-square=15.94 df=3 p=0.001 I^2 =81.2%

Test for overall effect z=1.75 p=0.08

HBOT for TBI

- **Conclusion in Cochrane Review:**
  - In people with TBI, the addition of HBOT significantly reduced the risk of death.
  - However, there is little evidence that more survivors have a good outcome.
  - The routine application of HBOT to these patients cannot be justified from this review.
  - In view of the modest number of patients, methodological shortcomings and poor reporting, this result should be interpreted cautiously.
  - An appropriately powered trial of high methodological rigor is required to define those patients (if any) who can be expected to derive most benefit from HBOT.

HBOT for TBI

- **Discussion:**
  - Outcome measures using Glasgow Outcome Scale (5 points scale) and further simplified into 2 categories (good or bad outcome) are too crude and insensitive to change. Further study using disability scale is needed.
  - HBOT need to be started in the early acute phase.

HBOT or Not?

Medical evidences

Patient's relatives' view

中國高壓氧專家蕭平田教授（右）昨日在講座上，跟朱振國的妻子（左）講解高壓氧治療法。

朱振國下周安排高壓氧治療

- 內地高壓氧專家說，朱現才接受高壓氧比較遲，但朱接受療程後「一定有進步」。

- 「如我是他的醫生，也會爲他做一做(高壓氧)，要有開發的思想，不能墨守成規，看看做後有何進展，無的話才放棄。」曾探望過朱振國兩次的蕭平田說，治療對他一定有幫助，說話可清晰一點，但康復程度則不能預測。「如不做的話，不可能好轉，若有其他感染，更可能會死亡。」

(明報 2006年5月31日)

家屬轟醫局漠視昏迷病人 兩年未獲腦科診症 指醫護說話涼薄

- 警員朱振國被襲受傷癱瘓事件，引起外界關注昏迷病人的治療權利。
- 社區組織協會連同4名昏迷病人的家屬昨日會見傳媒，批評醫院管理局對昏迷病人的檢查及診治不足，亦未有引入高壓氧、中醫等另類治療醫治昏迷病人，有病人等候超過兩年，也未能得到腦科醫生診症，更有醫護人員說話涼薄，令家屬甚難受。

(明報 2006年5月22日)

Michael Jackson's Bizarre Plan to Live to 150

- "I've taken several long naps in a hyperbaric oxygen chamber and when I awoke I felt like a new person - I've never felt better. …. I believe if I treat my body properly I'll live to be at least 150."
- Michael Jackson brought one monoplace hyperbaric oxygen chamber for use at home.

Contraindications

Contraindications of HBOT

Absolute C/I:

1. Untreated pneumothorax or lung collapse
2. Untested pacemakers
3. Selected medications
   - Doxorubicin, Bleomycin, Disulfiram, Cis-Platinum, Mefenide acetate.
4. Premature infants (cause retrolental fibroplasia)

Relative C/I:

1. Chronic sinusitis / URI
2. Seizure disorders
3. High fever
4. Severe COPD with CO_2 retention
5. Hx of spontaneous pneumothorax
6. Hx of thoracic surgery
7. Hx of surgery for otosclerosis
8. Hx of optic neuritis
9. Congenital spherocytosis & sickle cell disease
10. Pregnant
11. Active cancer conditions

Middle Ear Barotrauma

- Pain usu. occur during 1st 10fsw of descent.
- Preparation before diving:
  - Teach & instruct patient on equalization techniques:
    - Valsalva, Frenzel, Toynbee, jaw thrust, big yawn, swallow water, bend head to one side.
  - Exam ear & tympanic membrane movement.
  - Pre-medications: oral decongestants, antihistamines, topical vasoconstrictor sprays, steroid nasal sprays.
  - Myringotomy or insertion of pressure equalization tube.

Pulmonary Barotrauma

- Most dangerous but rare.
- Usu. on ascent when gas expands.
- Types:
  - Pneumothorax
  - Mediastinal emphysema
  - Subcutaneous emphysema
  - Traumatic gas embolism

Safety Issues

Safety Issues

- HBOT is generally safe providing the facility is properly installed and maintained, operators are properly qualified and trained, and therapy is conducted under medical supervision.
- Increases risk of fire in hyperbaric chamber:
  1. Lower ignition temperature under hyperbaric state.
  2. High O_2 content.
  3. Hyperbaric state speeds the burn rate.
  4. Risk of short circuit of equipment & battery.
  5. Inadequate staff training & maintenance in many countries.

Examples of Incidences

- 1996 (Japan): Monoplace chamber at 2.7 ATA 100% O2. Hand warmer in patient clothing caused ignition. Chamber exploded. Patient, his wife & 2 others killed. No attendant present outside chamber.
- 1997 (Italy): Multiplace chamber at 1.8 ATA (on descent). Liquid fuel warmer in pocket of patient caused ignition. Attempt to extinguish fire failed because fire suppression system not functional. 11 killed inside chamber.

Examples of Incidences

- 2001 (China): Multiplace chamber at 2 ATA air. Short in air-conditioning system caused ignition. Inside attendant (the only occupant) killed.
- 2002 (China): Monoplace chamber at 2 ATA 100% O_2. Cell phone taken by patient caused ignition. Patient killed.
- 2006 (Peru): Monoplace chamber at 2-2.5 ATA. Filled with air, O_2 by mask. Short in intercom system caused ignition. Patient killed. No attendant present.


Thank You !