Hyperbaric Oxygenation Questions and Answers

Refined and edited from published and unpublished research articles and email discussion.

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first, read how hyperbaric oxygenation works

The following document highlights current thought in some medical circles regarding hyperbaric oxygenation. To search for topics use your web browser "edit" function, pull down to "find" and type in your search term. This manuscript has research data from published work, some unpublished articles and some email discussion.

Q: Why is oxygen so important? A: Every day an average adult consumes 3 pounds of food, 3 pounds of water and almost 6 pounds of oxygen. People need about the same amount of oxygen by weight compared to food and water combined! From that 6 pounds of oxygen about 2 pounds gets into the blood for transport to tissue cells. We need this oxygen for the energy cycle that sustains life. When we do not have enough oxygen in our body tissues a series of events occur that if not corrected lead to disease conditions, either infection, tissue destruction or both. If there is low oxygen in tissues (hypoxia) there is a short window of opportunity to correct it. An excellent method to correct tissue hypoxia is by using a hyperbaric chamber. This web site is dedicated to making complex physiology easier to understand so we can make informed choices about health care.

What do you feel inside a hyperbaric chamber? Chamber atmosphere pressurization occurs slowly allowing you to adjust ear pressure changes. Yawning, swallowing or "blow the nose" clears ear pressure changes. Other than this ear pressure there are no unusual or different sensations.

What difference does extra pressure create? Hemoglobin (in red blood cells) holds 97% of its maximum amount of oxygen from normal air or holds 100% when breathing pure oxygen. One gram of hemoglobin can only combine with 1.34 ml of oxygen. Therefore, red blood cells can only deliver a limited level of oxygen to tissue cells, a pO2 of 39 mmHg or less. This is called oxygen tension (or oxygen partial pressure, "pO2") and is measured in units labeled "mmHg" (the amount of pressure able to raise the equivalent weight of a liquid mercury column. Injuries, infections and diseases can drop this vital tissue oxygen level down to almost zero! As we age we can loose vital lung capacity and the ability to effectively obtain adequate oxygen. Some disease conditions impair oxygen utilization. Also, injuries or conditions with swelling can cause pressure that cuts off circulation flow. This loss of blood flow, called ischemia, cuts off oxygen circulation to the affected areas of the body. This problem drops the pO2 gravely low, destroys tissue, and slows healing. Research has shown optimal tissue healing occurs if pO2 rises to between 50 and 80 mmHg. Oxygen given in a normal room is not sufficient to raise tissue oxygen levels to that level because red blood cells cannot carry the extra oxygen. The answer is to deliver the oxygen in a pressurized chamber to raise oxygen tension beyond red blood cell saturation.

How does being inside a pressurized chamber give us more oxygen? When we are inside a chamber pressurized at twice the normal air pressure it may not feel different, but we

breathe double the number of molecules. Breathing pure oxygen in such a chamber gives us 10 times the regular amount of oxygen. In one hour we can inhale about 2.4 pounds of oxygen. The extra oxygen dissolves directly into the blood fluid. In a few minutes this extra oxygen builds up tissue oxygen levels far above normal. This action has been scientifically proven to stimulate healing. In order to raise tissue oxygen tension above 50mmHg for optimal healing one must have oxygen delivered under increased atmospheric conditions. Look at the hyperbaric chart and observe the venous oxygen tension, which closely represents the final tissue oxygen tension, rise as we breathe oxygen beginning at 1.5 atmospheres of increased pressure. This marks the start of true hyperbaric pressure. Notice the phenomenal rise once atmospheric pressure increases twice above normal. This hyperoxia, increased tissue oxygen, is useful in healing.

What is the difference between saturation and oxygen tension? The problem we face in advocating proper usage of oxygen involves confusion between saturation and oxygen tension, 100% vs.. 100 mmHg. Only dissolved oxygen contributes to the tension (or partial pressure). Study the figures for oxygen transported by plasma (liquid) vs.. hemoglobin (one gram hemoglobin can only combine with 1.34 ml oxygen) - in 100ml of healthy blood there is 19ml oxygen as oxyhemoglobin and 0.3ml oxygen in liquid solution, here the hemoglobin is near maximum saturation (98%) and the pressure or tension of oxygen in the liquid solution is initially 95mmHg and downline tissue levels drop to 39mmHg or less. Breathing pure oxygen at 2.5 times atmospheric pressure increases the amount of oxygen in (plasma) liquid solution to about 6 ml per 100ml blood. This increased oxygen volume measurably increases the oxygen tension and downline tissue levels can rise upwards of 200mmHg.

Oxygen given with increased pressure can correct many serious health problems. Hyperbaric oxygenation helps the body heal from conditions that have low oxygen in the tissues causing or complicating the outcome. Repetitive hyperbaric sessions can help many different conditions; let's mention the first few ABC's such as anemia, burns and crush injuries. Compromised skin grafts often improve with hyperbaric oxygenation. Difficult to heal infections treated with hyperbaric oxygenation has attracted interest lately as antibiotic therapy can fail to clear today's resistant strains of pathogens. Treatable infections include such diverse situations as actinomycosis, osteomyelitis, diabetic wounds, gangrene and related deadly tissue infections. In the last four decades hyperbaric oxygenation research has raised the value of this unique therapy. Doctors used to ask, "Can it work?" now they ask, "How much is needed to completely work?"

Oxygen in Medical Practice: Oxygen is the most essential substrate for metabolism. We only function by oxidative metabolism and the reason for restoring blood flow to the brain with CPR is to establish an oxygen supply. See: OlesonSP. Brain Res 1986;368:24-29 also, JamesPB CalderIM JRSM 1991;84:493-495. Hypoxia (low oxygen levels in tissue) hinders healing. The sooner that tissue hypoxia is corrected the better the outcome. Many hypoxic tissues require hyperbaric pressure to achieve a significant increase in oxygen delivery because of poor oxygen solubility in blood. Despite thousands of publications, including controlled trials, attesting to the value of higher dosage oxygen, it is not widely practiced because:

I Oxygen transport is determined by the percentage respired and the barometric pressure: In normal hospital practice barometric pressure is ignored and it is assumed that patients receiving 100% are being given the same amount. In Denver Colorado which is at an altitude of over 5000 feet, the partial pressure is significantly lower than at sea level and a hyperbaric chamber is needed to give the same amount of oxygen as at sea level.

II Tissue hypoxia may be present in the absence of cyanosis: Oxygen supplementation is accepted in the alleviation of cyanosis, where the absolute level of deoxygenated hemoglobin exceeds 5g /100 ml of blood. However, the presence of cyanosis requires blood to be present in the microcirculation of a tissue and there can be significant hypoxemia without cyanosis when the hematocrit is low or when there is microcirculatory closure.

III Plasma oxygen transport is not limited by the saturation of hemoglobin: It is common for physicians to argue that blood is saturated with oxygen when a normal oxygen partial pressure (0.21 atm abs) is breathed at sea level. However it is not blood that is saturated, it is hemoglobin. The transport of oxygen by hemoglobin is finite as each of the ferrous receptor sites on the molecule can only bind one oxygen molecule. However, the plasma oxygen content increases directly as a function of the inspired partial pressure of oxygen. Breathing pure oxygen at twice atmospheric pressure, the plasma oxygen content is ten times the value of breathing air at sea level and life can be sustained without hemoglobin (continued consciousness may need higher pressure).

IV Oxygen transport to tissue depends on the tension of oxygen in plasma: Severe tissue hypoxia can be present when arterial oxygen tensions are normal if local circulatory factors, such as arterial occlusion, closure of the microcirculation and edema are present. An increase in the water content of tissue limits oxygen transport. If inflammation, edema and the invasion of metabolically active inflammatory cells occur at the same time, we can have hypoxia even when the blood flow per unit volume of tissue is increased, hence hyperemic hypoxia. In hyperbaric conditions the oxygen plasma tension increases from values of 95mm Hg to over 2000 mm Hg increasing the gradient or the transfer of oxygen into tissues by 20 fold.

V Normal blood flow does not ensure normal oxygenation: Oxygen delivery requires blood flow, although blood flow may be normal and the tissue still hypoxic. The only tissue that does not need blood flow for oxygenation is the lung.

VI Oxygen is not "Hyperbaric": The use of the term "hyperbaric" may appear to imply that the oxygen delivered is different to the molecular oxygen available from the air. People may think of it as singlet oxygen 01 or ozone 03, perhaps some regard hyperbaric oxygen as 04. The correct terminology is hyperbaric oxygenation or hyperoxia. The psychology of the word "hyperbaric" indicates a potential marketing problem.

VII The adjunctive nature of most oxygen supplementation: Oxygen may be a primary treatment in some instances, but the impression is often given that oxygen therapy replaces other treatment. In most cases this is incorrect, other therapy is needed and optimal care is not a competition between therapies.

VIII Hypoxia, not oxygen, causes oxygen free radicals: Here is an important, often misunderstood point. Contrary to prevailing misinformation it is hypoxia that mediates the

release of oxygen free radicals. An inadequate oxygen supply to tissue results in the catabolism of ATP to adenosine and the creation of an electron donor, xanthine. When oxygen is made available the electron is accepted to form the superoxide anion 02. It is important to recognize that hypoxia causes a cascade of interactions that generate hydroxyl ions which damage membranes and draws calcium into the cell. Correcting hypoxia will limit this free radical formation. Many physicians tend to think oxygen causes oxidative damage, quite the contrary, it is the lack of oxygen that causes the damage. Reperfusion injury occurs when circulation is cut then returned with poorly oxygenated blood flow. Somehow oxygen gets blamed for this, yet if one has benefit of hyperbaric oxygenation we see a dramatic reduction in reperfusion damage.

IX Hyperoxia and oxygen toxicity: It is well known that exposure to pure oxygen for a prolonged period, that is, in excess of 24 hours at 1 atm abs causes reversible damage to the endothelium of pulmonary capillaries. Short term exposure to very high oxygen pressures, for example, over 3 ATA for 2 hours may cause convulsions resembling grande mal epilepsy. The time to convulsion is reduced by exercise or an increased metabolic rate. However, clinical use of hyperbaric oxygen uses a well-defined exposure limit that prevents this. The sites where autoregulation may fail to limit blood flow are the ends of fingers and toes. This is because arteriovenous shunts are present to return blood in vasodilatation and results in blood flow which is greatly in excess of tissue requirements. Toxicity to peripheral nerve endings is often manifest as parasthesia. Pre-existing epilepsy does not lower the threshold to oxygen toxicity. In fact, epilepsy can be treated with hyperbaric oxygenation and many of the 12,000 patients in our UK MS charity have epilepsy. We have not had a convulsion in our 16 years of operation. See: Qibiao W, et al. Treatment of children's epilepsy by hyperbaric oxygenation; analysis of 100 cases. Proc 11th International Congress on Hyperbaric Medicine. Best Publishers. 79-81. We have looked at trancutaneous values and they are linear to 2 atm abs but there is a wide distribution after that. No long term sequelae have been described after oxygen convulsions. Oxygen convulsions were used in place of electric shock therapy in the 1950's in the USA.

X Unfamiliar technology: Hyperbaric medicine is not generally familiar to most physicians because it is rarely taught in medical schools. Those who are involved have generally come from the fields of aviation or diving. As both of these disciplines use high technology, it is not surprising that hyperbaric oxygen itself is viewed in this light. However, the pressures used clinically, up to a maximum of 2.5 ATA, are very modest in comparison to the maximum human experimental pressurisation of 71 atm abs. Unfortunately, even physicians familiar with hyperbaric medicine refer to "fitness to go under pressure," forgetting that we are all subject to normal atmospheric pressure. Also, it is outside our pharmaceutical paradigm in the west. In other cultures it has been more readily accepted. The HBO2 approach has largely come after the tablet/injection approach was developed and therefore to take a place in healthcare, HBO2 must produce proof of improvement above that already obtained. HBO2 has to jump higher "proof" hurdles.

XI Finance: The pressure against a 30" hyperbaric chamber hatch at 2 atmospheres is 5 tons! This requires a chamber certified to safely hold the high pressure. The use of increased pressure requires a hyperbaric chamber and therefore some financial investment.

In the case of a walk-in multiplace chamber this can be considerable and there are usually building modifications required. Plus, there is no commercial promotion of oxygen in the pharmaceutical sense to make physicians aware of hyperbaric oxygenation's value. This will not change and is a major reason for the slow growth of oxygen as a therapy. No promotion without a patent! No matter how much scientific evidence we produce we need marketing and no one will make that investment without a return. We have more scientific evidence about actions and mechanisms supporting the correction of tissue hypoxia than any pharmaceutical product.

XII Misunderstandings: It is very clear there is a general failure to understand the fundamental importance of oxygen in human physiology. If this were not the case, HBO2 would already have become just another tool used in the day-to-day practice of medicine as are pills, surgical knives and injections. Perhaps a major barrier to gaining greater acceptance within the medical community at large is the persistence in referring to clinical HBO2 treatments as "dives". Diving and clinical hyperbaric medicine are not the same thing. Diving relates to underwater military, commercial or amateur activities, recompression is necessary when things go wrong, it is not a choice if you wish to resolve a DCS problem. In clinical applications patients do not go anywhere near the water (in my experience a lot of people think they do), they are pressurized for the specific purpose of increasing tissue oxygen tensions in order restore or assist the healing process. The term "fitness to dive" is another diving term and relates to the ability of an individual to deal with the physiological stress of deep diving and working underwater. The whole objective of pressurizing a clinical patient is to increase tissue oxygen tensions in conditions where HBO2 is beneficial. This would not be necessary if they were "fit". A patient in a chamber breathing 100% oxygen is under less physiological stress rather than more because of the benefits derived from the oxygen. Someone raised the point about pneumothorax expanding on decompression - this does not apply because breathing oxygen actually reduces the volume of a pneumothorax by increasing the inherent unsaturation and gradient for nitrogen elimination. The risk of ear squeeze associated with hyperbaric treatment is manageable, just slow down rate of pressure change or insert grommets. It is not "fitness to dive" that is the issue, just responsible medical practice. Our rate of impending or actual aural barotrauma (ear pain) requiring aborting of a treatment on compression is about 3% of total attempted treatments. This at least in part reflects our patient population. We have a high proportion of people with a history of head and neck irradiation and eustachian tube dysfunction, complex head and neck surgery and those with residual CNS depression from drugs. Calling hyperbaric sessions "dives" contributes to the underuse of HBO2 and reflects the involvement with those of us who have entered the field from diving. Diving is entering water, we are not immersing patients in water! Many talk about delivering oxygen under pressure - being a gas it is impossible to deliver without pressure. We deliver oxygen with INCREASED pressure. Also, the use of a pretreatment radiograph of the chest is unnecessary - it is not even predictive in submarine escape training where the decompression rate can be 0.25 atm a second. I must say that I despair when physicians have difficulty accepting the idea that the sooner we correct hypoxia the better the outcome. The excellent studies of Zamboni's group indicate the importance of a very large oxygen concentration in modifying the changes induced by ischemic hypoxia. In our experience of over 1.25 million sessions in the last sixteen years the specific pressure does not appear to be so critical. I cannot [see the basis of fears about pressure distinctions]. One patient I

treated in 1981 had a massive leg injury in Borneo and arrived back in the UK after eleven weeks in the Shell base hospital in Penaga. There were 17 bone fragments between his knee and ankle and a large amount of soft tissue damage. I used 2 ata for 90 minutes twice daily. The space between the tibial fragments after fixation was 1.25 inches and new bone bridged this in four weeks of therapy. He had a total of 254 sessions of HBO2 and thirteen operations. The key issue in fractures is - what are the tissue and bone oxygen tensions? Nilsson and co-workers in Gothenburg used 2.8 atm for two hours daily in their study of bone healing in rat mandibular osteotomies. They found twice the rate of healing in the HBO2 group there was also reduced damage in the incisor pulp, odontoblasts and enamel organ. The successful Marx protocol uses 2.4 atm abs. - Dr. Philip James, Wolfson Hyperbaric Medicine Unit, University of Dundee, Ninewalls Medical School. Dr. Philip James was trained in general medicine, involved in vascular research before specializing in occupational medicine. Over the last 25 years has been involved in the study of acute neurological syndromes associated with decompression sickness. He became interested in the effects on the nervous system after witnessing them first hand in decompression trials and then being involved in the acute treatment of divers working in the North Sea. He worked with Prof. Brian Hills the biomedical scientist now living in Brisbane. In persuing this area in the University of Texas and in Texas A&M University they researched a number of aspects of spinal cord function and pathophysiological mechanisms including microembolism. They also did research into the blood-brain barrier and its stabilization by adsorbed surfactant and mechanisms of disruption. The message is that although blood-brain barrier function is well understood by the drug industry it has been ignored by neurologists who are rarely in a position to do any fundamental research. If tissue barriers are disrupted then the secondary effect is the activation of aseptic inflammation due the extravasation of protein and an immune response - directed at damaged host tissue - the so-called "auto-immune" response. Over the last ten years they have looked at experimental inflammation in a human model and the role of hypoxia and hyperoxia. The focus centers on treatment of microembolism with hyperbaric oxygenation.

For most physicians hemoglobin saturation has become a constant and a clinical endpoint. Oxygen saturation and oxygen tension have similar numbers attached - 100% (saturation) and 100 mm Hg (tension) . This is is re-inforced by statements which draw attention to the small volume of gas carried in physical solution. In the reference text Scientific Tables, published by JR Geigy SA Basle, the section on blood gases states: "The oxygen in physical solution is often ignored and the oxygen capacity equated with the amount capable of being bound by the hemoglobin." The quantities for 100 ml of blood breathing air at sea level with an arterial oxygen tension of about 95 mm Hg are 19 ml bound as oxyhemoglobin and 0.3 ml in physical solution. However it is only the oxygen in physical solution that is available for transport to the tissues and although the volume of oxygen bound to hemoglobin is large it is not all readily available. The normal arterial - venous difference is only about 5ml per 100ml of blood at rest, which means that about 14 ml per 100 ml of blood is still present after blood has circulated. The ability of tissues to remain viable depends on a minimum level of oxygen availability. It is not possible to maintain normal brain function as the plasma oxygen tension falls below 40 mm Hg, but at this tension the arterial saturation is 75% and arterial blood still contains 13.8ml per 100 ml blood. Philip James - Reference: Haldane JS, Meakins JC, Priestly JG. J Physiol 1918-19;lii::420

Question about possible complication: Someone raised the point about pneumothorax expanding on decompression - this does not apply because breathing oxygen actually reduces the volume of a pneumothorax by increasing the inherent unsaturation and gradient for nitrogen elimination. (Just breathe 100% oxygen during decompression.)

Why HBO2 chambers are not in every doctor's clinic: It is very clear there is a general failure to understand the fundamental importance of oxygen in human physiology. If this were not the case, HBO2 would already have become just another tool used in the day-to-day practice of medicine. Perhaps a major barrier to gaining greater acceptance within the medical community at large is the persistence in referring to clinical HBO2 treatments as "dives". Diving and clinical hyperbaric medicine are not the same thing. Diving relates to underwater military, commercial or amateur activities, recompression is necessary when things go wrong, it is not a choice if you wish to resolve a decompression sickness problem. In clinical hyperbaric applications patients do not go anywhere near the water (in my experience a lot of people think they do), they are pressurized for the specific purpose of increasing tissue oxygen tensions in order restore or assist the healing process. The term "fitness to dive" is another diving term and relates to the ability of an individual to deal with the physiological stress of deep diving and working underwater. The whole objective of pressurizing a clinical patient is to increase tissue oxygen tensions in conditions where HBO2 is beneficial. This would not be necessary if they were "fit". A patient in a chamber breathing 100% oxygen is under less physiological stress rather than more because of the benefits derived from the oxygen. A simple risk analysis suggests to me that the risk of ear squeeze associated with hyperbaric treatment, is considerably less than risk associated with radical surgery, limb loss or death from multiple organ failure. There are many precautions that can be taken to reduce the risk associated with treatment in any medical modality, clinical HBO2 is no different. Slow down rate of pressure change, insert grommets and give vitamin E are just a representative sample. It is not "fitness to dive" that is the issue, just responsible medical practice. Our rate of impending or actual aural barotrauma (ear pain) requiring aborting of a treatment on compression is about 3% of total attempted treatments. This at least in part reflects our patient population. We have a high proportion of people with a history of head and neck irradiation and eustachian tube dysfunction, complex head and neck surgery and those with residual CNS depression from drugs. Calling hyperbaric sessions "dives" contributes to the underuse of HBO2 and reflects the involvement with those of us who have entered the field from diving. Diving is entering water, we are not immersing patients in water! Many talk about delivering oxygen under pressure - being a gas it is impossible to deliver without pressure. We deliver oxygen with INCREASED pressure. Also, the use of pretreatment chest radiograph is unnecessary - it is not even predictive in submarine escape training where the decompression rate can be 0.25 atm a second. I must say that I despair when physicians have difficulty accepting the idea that the sooner we correct hypoxia the better the outcome. The excellent studies of Zamboni's group indicate the importance of a very large oxygen concentration in modifying the changes induced by ischemic hypoxia. In our experience of over 1.25 million sessions in the last sixteen years the specific pressure does not appear to be so critical. I cannot [see the basis of fears about pressure distinctions]. One patient I treated in 1981 had a massive leg injury in Borneo and arrived back in the UK after eleven weeks in the Shell base hospital in Penaga. There were 17 bone fragments between his knee and ankle and a large amount of soft tissue damage. I used 2 ata for 90 minutes twice daily. The space between the tibial

fragments after fixation was 1.25 inches and new bone bridged this in four weeks of therapy. He had a total of 254 sessions of HBO2 and thirteen operations. The key issue in fractures is - what are the tissue and bone oxygen tensions? Nilsson and co-workers in Gothenburg used 2.8 atm for two hours daily in their study of bone healing in rat mandibular osteotomies. They found twice the rate of healing in the HBO2 group there was also reduced damage in the incisor pulp, odontoblasts and enamel organ. The successful Marx protocol uses 2.4 atm abs. Philip James, Wolfson Hyperbaric Medicine Unit

Q: Is HBO2 risky? A: Dr. Philip James' notes in 1999 their hyperbaric facilities have safely done over 1.2 million patient sessions without incident. He says that, "Engineering standards are of primary importance but adequate training for the operation of chambers in a non-acute setting requires only basic information. There is no maximum number of treatments.

Q: Is there any reason to believe that the beneficial effects of HBO2 would continue beyond treatment endpoint? If so, approximately how long and why? A: Barr and Perrins published some observations on this matter in the Proc.11th International Congress 1995 (ISBN 0-941332-44-6). Briefly, they showed tissue oxygen partial pressure measurements that rose from near zero to 50 mmHg after some months long course of HBO2 were retained without further treatment for at least three years! They thought they were witnessing a vascular 'medical disobliteration'. Whether this is due to recanalization of atrophied vessels or in-growth of neovasculature is open to question.

Q: Do you have any information about Crohn's Disease Tx with HBO2? A: Brady CE et al. healing of severe perineal and cutaneous Crohn's disease with hyperbaric oxygenation. Gastroenterology 1989;97:756-60. Also, Nelson EW, et al. Closure of refractory perineal Crohn's lesion; integration of hyperbaric oxygenation into case mangement. Digestive Diseases and Sciences 1990;35:1561-1565. Brady CE et al. healing of severe perineal and cutaneous Crohn's disease with hyperbaric oxygenation. Gastroenterology 1989;97:756-60. Gastroenterology 1989 Sep;97(3):756-60 Healing of severe perineal and cutaneous Crohn's disease with hyperbaric oxygen. Brady CE 3d, Cooley BJ, Davis JC Division of Gastroenterology, University of Texas Health Science Center, San Antonio. Recurrent perineal Crohn's disease can be an extremely debilitating complication that may be difficult to treat. We report a patient with progressively worsening perineal and biopsy-proven cutaneous Crohn's disease that had been refractory to surgery and medical treatment (sulfasalazine, steroids, 6-mercaptopurine, metronidazole, antibiotics). As the lesions were reminiscent of problem wounds occurring in other situations, hyperbaric oxygen treatment was instituted while the patient was continued on metronidazole. Response was dramatic with almost immediate relief of symptoms and regression within 2.5 mo of wounds that had previously defied therapy for 8 yr. Clinical remission has not been sustained as four subsequent courses of hyperbaric oxygen have been given over a period of 11 mo. However, the patient has been essentially asymptomatic since her initial course and the extent of her cutaneous disease has been minimal compared with that before hyperbaric oxygen. Hyperbaric oxygen treatment is costly and should not be routinely used in every patient with perineal Crohn's disease. However, this case report may herald an advance in the understanding of the pathogenesis of this complication and ultimately, its therapy. Gut 1998 Oct;43(4):512-8 Hyperbaric oxygen: a novel modality to ameliorate experimental

colitis. Rachmilewitz D, Karmeli F, Okon E, Rubenstein I, Better OS Departments of Medicine and Pathology, Hadassah University Hospital, Mount Scopus, Hebrew University-Hadassah Medical School, Jerusalem, Israel. BACKGROUND: Hyperbaric oxygen (HBO) has been suggested to be beneficial in inflammatory bowel disease but the mechanisms responsible for its therapeutic effects have not been elucidated. AIM: To assess the effect of HBO treatment on colonic damage in two models of experimental colitis, and to examine whether this effect is mediated by modulation of NO synthesis. METHODS: Colitis was induced by either flushing the colon with 2 ml 5% acetic acid or intracolonic administration of 30 mg trinitrobenzenesulphonic acid (TNB) dissolved in 0.25 ml 50% ethanol. Rats were exposed to HBO (100% oxygen at 2.4 atmosphere absolute) for one hour twice on the day of colitis induction and once daily thereafter. Control rats were treated only with acetic acid or TNB. Rats were killed 24 hours after acetic acid administration or one and seven days after TNB treatment. The colon was isolated, washed, and weighed, the lesion area was measured, and mucosal scrapings were processed for determination of myeloperoxidase (MPO) and NO synthase (NOS) activities, prostaglandin E2 (PGE2) and leukotriene B4 (LTB4) generation. RESULTS: In control rats exposed for seven days to HBO2, colonic NOS activity was significantly decreased by 61%, compared with its activity in untreated rats (2.93 (0.17) nmol/g/min). HBO2 significantly reduced by 51 and 62% the extent of injury induced by acetic acid and TNB respectively. The protection provided by HBO2 was accompanied by a significant decrease in colonic weight, PGE2 generation, MPO, and NOS activities. In acetic acid colitis, LTB4 generation was also significantly decreased. CONCLUSIONS: (1) HBO2 effectively decreases colitis induced by acetic acid and TNB. (2) The decreased NOS activity induced by HBO2 suggests that reduction in NO generation may be among the mechanisms responsible for the anti-inflammatory effect of HBO2. (3) HBO2 may be considered in the treatment of patients with refractory inflammatory bowel disease. See also: Nelson EW, et al. Closure of refractory perineal Crohn's lesion; integration of hyperbaric oxygenation into case mangement. Digestive Diseases and Sciences 1990;35:1561-1565.

I was at medical school just after the role of oxygen in producing blindness in premature neonates in the 1950s had been fully established and hammered home in teaching. After nearly 40 years I now know that IT IS WRONG. Yesterday I was astounded to find these details in a letter from RM Forrester:- Szewczyk first suggested that retrolental fibroplasia was produced by habituating a child to an enriched oxygen atmosphere and by too sudden withdrawal. If Szewczyk's theory was correct the disease in the early stage should appear after the child's removal from a high oxygen environment; this is, almost without exception, true. The next logical step was to say that if the retinopathy developed when the child came out of oxygen the safest thing to do would be to put him back in again. We used this technique in 17 cases. The results were SPECTACULAR; in each individual case the retinal vascular pattern, having shown gross abnormalities, returned to normal. In most cases a slow reduction of oxygen and final return to atmospheric concentration over a period of weeks was all that was necessary, but two infants needed a third period of oxygen exposure because the disease again became active. Many of the infants were exposed to high oxygen tensions for very long periods (the longest were 93, 88, 85 and 83 days) Twelve of these 17 infants recovered with normal eyes and five had minor permanent changes not causing blindness. If one believes that oxygen has a direct toxic effect on the infant's retina these surely would have been the infants who became blind for they were all

of very low birth weight, all had the early retinopathy and they were all subjected to intensive and prolonged therapy. Forrester RM Letter to the editor Dev Med Child Neurol 1964;6:648-650 Alison McDonald had already made the point that oxygen protects against cerebral palsy :- 1 of 16 children born in 1950 to 1952 had cerebral palsy and 4 had retrolental fibroplasia 10 of 25 born in 1953-1955 had cerebral palsy and None had retrolental fibroplasia ($p<0.02$) Significance for increase in CP without additional oxygen ($p< 0.05$) Significance of reduction of retrolental fibroplasia without additional oxygen ($p<0.02$) Alison D McDonald Dev Med Child Neurol 1964;6:313-314. Hundreds of thousands of children have died or consigned to a lifetime of disability simply because we have neglected to use oxygen properly. We have a duty to see that this terrible mistake is corrected Philip James, Wolfson Hyperbaric Medicine Unit, University of Dundee Detailed report: Retrolental Fibroplasia Correction - Dr. Philip James

Commentary: Evidence that retinopathy of the newborn is due to hypoxia not oxygen toxicity. The introduction of tents and incubators following World War II allowed premature infants to be given supplementary oxygen to improve their chances of survival and levels up to 80% were often given for extended periods. Many cases of blindness followed (1) and led to a restriction of the level of supplemental oxygen to 40%, which dramatically reduced the incidence of retinopathy. This confirmed the involvement of oxygen and since then every medical student has been taught that the retinopathy of the newborn is caused by oxygen toxicity. However, a Lancet editorial in 1992 (2) observed that the use of continuous transcutaneous monitoring to avoid even transient hyperoxia has failed to abolish retinopathy in neonates and discussed the evidence that restricting the use of additional oxygen adversely affects mortality. Despite many improvements in neonatal care cerebral palsy also remains a serious problem and it is relevant that McDonald (3) noted a statistically significant rise in the incidence of cerebral palsy with the reduction of oxygen levels. Of 16 children born from 1950 to the end of 1952, when levels of 60-80% oxygen were used, she found that only 1 of 16 children developed cerebral palsy with four developing retrolental fibroplasia. In the following three years, when incubator levels were reduced to 40%, 10 of 25 children developed cerebral palsy ($P<0.05$) and none developed retinopathy. ($P<0.02$) McDonald commented "unfortunately it may prove impossible to prevent spastic diplegia by increasing the ambient oxygen concentration without causing retrolental fibroplasia." Critical evidence has been overlooked. In 1951 Szewczyk 4 suggested that retinopathy of the premature was produced by too rapid a reduction of the level of oxygen when a child had been habituated to an enriched oxygen atmosphere. He returned infants with a developing retinopathy to a high oxygen level and reversed the changes. He then slowly reduced the oxygen concentration to establish air breathing. A small controlled trial was undertaken (5) with 24 premature infants being slowly reduced to a normal atmospheric concentration and 26 abruptly withdrawn. Only 2 infants in the first group developed retinopathy, compared to 13 in the second ($p<0.001$) but the study was criticised because the infants who were in the weaned group actually had less oxygen overall. Nevertheless, it appears that the investigators only undertook the study because they knew that the retinopathy could be reversed by re-exposing the infants to a raised partial pressure of oxygen. Jefferson, (6) following the report by Szewczyk, also returned infants developing retinopathy to a high level of oxygen and described the results in the first six infants as "dramatic." She observed that the speed with which the changes were reversed greatly exceeded the rate at which spontaneous regression occurs. The vascular

engorgement disappeared within 48 hours, capillary tufts ceased to be visible and retinal oedema subsided. Forrester (7) continued this approach and wrote that the effects were "spectacular; in each individual case the retinal vascular pattern, having shown gross abnormalities, returned to normal." Again a slow reduction of the oxygen level to an atmospheric concentration was used, but two infants in a series of 17 needed a third period of exposure, because the disease again became active. Twelve recovered with normal eyes and five had minor permanent changes not causing blindness. Many of these infants were exposed to high oxygen concentrations for very long periods (the longest were 93, 88, 85 and 83 days). He commented; "if one believes that oxygen has a direct toxic effect on the infant's retina these surely would have been the infants who became blind, for they were all of very low birth weight, all had the early retinopathy and they were all subjected to intensive and prolonged therapy." Others made the same observations. (8,9) but by 1955 a large multicentre study (10) was published comparing the rates of retinopathy between high and low oxygen concentrations. It proved that the retinopathy was linked to high levels of oxygen, but it did not establish that it was due to toxicity. The sequence of the vascular changes suggests that the retinopathy is due to hypoxia and the only established risk factors in retinopathy of the premature are conditions associated with intrauterine hypoxia. (11,12) Initially the retinal vessels dilate becoming tortuous and this is followed by oedema and haemorrhage. Vascular dilatation with increased permeability occur in response to hypoxia and diapedetic haemorrhage indicates gross impairment of the blood-retinal barrier. The developing oedema will begin to separate the retina and also impair oxygen transport. Because the retina is applied to the concave hemisphere of the globe of the eye it is reasonable to suggest that the tortuosity of the vessels occurs because the scleral tissues are inelastic and mechanical distortion contributes to retinal detachment. If this is the case, then increasing the plasma oxygen tension, which can paradoxically induce vasoconstriction whilst increasing the gradient for oxygen transport, would be expected to reverse the condition as described. Supporting evidence has recently been provided. Lewis et al (13) have studied the effect of oxygen supplementation in an experimental model of retinal detachment based on the premise that hypoxia is involved both in the death of photoreceptors and the glial reaction. They found that oxygen supplementation to 70% - the level used to treat retinopathy in the newborn - reduced photoreceptor death and limited the proliferation of the retinal Muller cells responsible for gliosis. The oxygen tension determines the capillary density in a tissue, even in the adult mammalian brain. Rats decompressed to half atmospheric pressure for three weeks increase the capillary density in the brain by 50%. (14) This mechanism is part of the adaptation that allows climbers to ascend to very high altitudes, such as Mount Everest, without supplementary oxygen. Hyperoxia has the opposite effect in the developing retina. Ashton et al (15) demonstrated that oxygen supplementation suppressed the development of the retinal circulation in an experimental model and they suggested using high levels of oxygen intermittently. This has been clinically successful. (16,17) The circulation of both the brain and the retina mature rapidly in the last few weeks of pregnancy (18) and the maintenance of hyperoxia would predictably suppress vessel formation, not because of oxygen toxicity, but simply the prevention of hypoxia. This data demands urgent reappraisal because it is clear that oxygen therapy is indicated in retinopathy of newborn and may also provide the much sought after intervention in hypoxic-ischemic encephalopathy. Magnetic resonance spectroscopy has shown the relationship between cerebral hypoxia and poor neurological outcomes in neonates.19 For the growing infant, oxygen is friend not foe. P B James PhD FFOM W B

Haining FRCS (Ed), FRCOph References: 1. Forrester RM, Jefferson E, Naunton WJ. Oxygen and retrolental fibroplasia; a seven-year survey. Lancet 1954;ii:258-60. 2. Editorial. Oxygen restriction and retinopathy of prematurity. Lancet 1992;339:961-62. 3. McDonald AD. Oxygen Treatment of Premature Babies and Cerebral Palsy. Dev Med Child Neurol 1964;6:313-14. 4. Szewczyk TS. Retrolental fibroplasia: etiology and prophylaxis. Amer J Ophthalmol; 951:34:1609. 5. Bedrossian RH, Carmichael P, Ritter J. Retinopathy of prematurity (retrolental fibroplasia) and oxygen. Amer J Ophthalmol 1954;37:78-86. 6. Jefferson E. Retrolental fibroplasia. Arch Dis Child 1952;27:329-36. 7. Forrester RM. Oxygen cerebral palsy and retrolental fibroplasia. Dev Med Child Neurol 1964;6:648-50. 8. Swart-Van Der Hoeven JT, Mak, TMB. Effects of oxygen on retrolental fibroplasia in premature infants, with report of two cases. Maadschr Kindergeneesk 1952;20:276-77. 9. Von Winning, CHOM. Retrolental fibroplasia and other forms of pseudoglioma. The Hague Drukkerij Trio, 1952. 10. Kinsey VE. Retrolental fibroplasia. Co-operative study of retrolental fibroplasia and the use of oxygen. Arch Ophthalmol 1955;59:481-542. 11. Bruckner HL. Retrolental fibroplasis associated with intrauterine anoxia. Arch Ophthmol 1968;80:504-505. 12. Johnson I, Schaffer DB, Blessa MI. Factors predisposing to RLF: complications of pregnancy. Pediat Res 1980;14:601. 13. Lewis G, Mervin K, Valter K, Maslim J, et al. Limiting the proliferation and reactivity of retinal Muller cells during experimental retinal detachment: the value of oxygen suplementation. Am J Ophthalmol 1999;128:165-72. 14. Harik SI, Behmand RA, LaManna JC. Hypoxia increases glucose transport at blood-brain barrier in rats. J Appl Physiol 1994;77:896-901. 15. Ashton N, Garner A, Knight G. Intermittent oxygen in retrolental fibroplasia. Am J Ophthalmol 1971;71:153-60. 16. Valk LEM, Tiddens H. A case of retrolental fibroplasia, treated and cured with administration of oxygen in alternating concentrations. Ophthalmologica 1960;139:475-78. 17. Tanabe Y. Intermittent oxygen for the treatment of the retinopathy of prematurity. Nippon Ganka Gakkai Zasshi 1972;76:5 316-21. 18. Takashima S, Tanaka K. Development of cerebrovascular architecture and its relationship to periventricular leukomalacia. Arch Neurol 1979;35:11-16. 19. Ashwal S, Holshouser BA, Tomasi LG, Shu S, et al. 1H-magnetic resonance spectroscopy-determined cerebral lactate and poor neurological outcomes in children with central nervous system disease. Ann Neurol 1997;41:470-81.

Q: How important is early intervention with high dosage oxygen therapy? A: The problem with oxygen in acute emergency therapy involves the timing of the high dose administration. This is critical because the secondary events follow an exponential curve of increasing severity. If treatment is delayed then the efficacy become more and more difficult to establish, primarily because an elevated arterial oxygen tension is not reflected at tissue level which is where it matters. Incidently a high concentration of oxygen actually prevents CO poisoning and yes, I do have the reference! Dr. Philip James

Q: Why is a PaO2 of 400mmHg better than 95mmHg? A: The data is vast - and is the fundamental basis for the use of hyperbaric oxygenation. Think about wound healing. Given a plasma oxygen tension of 95 mm Hg and a tissue oxygen tension in a diabetic foot of say 10 mm Hg. This level of oxygen is below the limit for viability and the tissue will become necrotic. Giving oxygen under hyperbaric conditions increases the gradient for transfer into the tissues and so a plasma tension of 400 mm Hg may achieve a tissue oxygen tension in the same patient of 60mm Hg - well within the limits of viablity. The astonishing

thing is that serial hyperbaric oxygen therapy actually allows capillary neogenesis which is stimulated by a mild degree of hypoxia but stopped altogether (as are most other things) by a severe degree of hypoxia.

Q: Is it unreasonable to ask that an expensive, limited availability resource like HBO2 should be required to show more benefit when compared to less expensive traditional medical methods? A: HBO2 need not be expensive. For example wound care can be achieved by a nurse or physiotherapist in a simple chamber. Cost benefit analyses have shown, for example in burns, that even given the very high costs of HBO2 in California (technical cost of $500 per hour) it still saves money to use it.

Q: Is high dosage oxygen proven? A: Do you regard the administration of 100% oxygen at 1 atm abs as proven? In this case if the patient improves with this arterial value then you must also regard this treatment as proven. Proven to do what? Restore consciousness - relieve breathlessness. I think this makes a lot of sense and probably explains our difficulty in showing a clear benefit in the trials I cited previously. The efficacy becomes more and more difficult to show because it may no longer be there. Answer: do a better trial. Study the Rockswold controlled study of head injury in the Journal of Neurosurgery 1992 vol 76 929-934. No patient was treated in the first six hours because of delays by transportation resuscitative measures and the randomisation protocol. The mortality in the HBO2 treated group was halved. Please note the adacemic nonsense of including in the treated group patients who were not given HBO2 and the initial failure to use myringotomy. When you see patients wake up when given oxygen - whether it be in a chamber or not then it is evidence that more oxygen was needed just as in hypovolaemic shock IV infusion resores blood pressure. In evidence based medicine it is accepted that agents like adrenaline which result in an immediate reversal of a condition do not require randomised controlled trials. The reference is: Haldane JS. The relation of the action of carbonic acid to oxygen tension. J Physiol (Lond) 1895;18:201-217.

Controlled Clinical Trials of Hyperbaric Oxygenation:

1. Carbon monoxide poisoning: Goulon et al (1969). Mortality compared when HBO2 given before and after 6 hours. Ann Méd Interne (Paris). 120:335-349. Pace et al. (1950). Clearance rate of CO accelerated. Science. 111:652-4. Ducassé et al. (1988). Normobaric O2 v HBO2. Faster recuperation and fewer EEG abnormalities after 3 weeks. Proc. 2nd Swiss Symposium. Normobaric and hyperbaric oxygen treatment of acute carbon monoxide poisoning in rats. Undersea Hyperb Med 1997 Jun;24(2):107-116 Jiang J, Tyssebotn I; Department of Physiology, University of Bergen, Norway. Based on a model of acute carbon monoxide (CO) poisoning in rats with an occluded left carotid artery, we have evaluated the effects of normobaric oxygen (NBO2) and hyperbaric oxygen (HBO2) on mortality and morbidity. After exposure to 2,700 ppm CO in air for 1 h, the rats were grouped and treated with air (group 1, untreated controls, in a previous study), 100 kPa O2 for 4 h (group 2), 300 kPa normoxia (group 3, pressure controls), and 300 kPa O2 (group 4) for 1 h, respectively. NBO2 started immediately, whereas HBO2 began 35 min after the end of the CO exposure. At the termination of the exposure, the four groups suffered identical levels of poisoning as indicated by the degrees of hypothermia, hypocapnia, drop in mean arterial pressure, and acidosis. Up to 48 h after the end of the CO exposure, mortalities were 76, 58, 75, and 17 in groups 1-4, respectively. The neurologic morbidities,

indicated by abnormal motor behaviors and edema in the left cerebral hemispheres, were 84, 67, 83, and 42% in groups 1-4, respectively. Compared to the normoxic treatments, the HBO2, but not the NBO2, significantly reduced the mortality and the neurologic morbidity. HBO2 was also significantly better than NBO2 in increasing surviving time and survival rate. The results support the value of HBO2 in improving short-term outcome of acute CO poisoning in this rat model.

2. Gas Gangrene: Bakker (1988). Amputation rate 8% cf 50-60% without HBO2. In: Problem Wounds - role of Oxygen. Elsevier pp 153-172.

3. Free Skin Grafts: Perrins (1967). With HBO2 92% of grafts survived, 63% in Controls. Lancet ii:868-871

4. Burns: Hart et al. (1974) Healing time, morbidity, and mortality significantly reduced. Surg Gynaecol Obstet. 139:693-6.

5. Leg Ulcers: Hammarlund C & Sundberg T. (1994). Hyperbaric oxygen reduced size of chronic leg ulcers: a randomised double-blind study. Plastic & Reconstructive Surgery. 829-834.

Brown recluse spider envenomation: a prospective trial of hyperbaric oxygen therapy. Acad Emerg Med 1997 Mar;4(3):184-192; Maynor ML, Moon RE, Klitzman B, Fracica PJ, Canada A; Department of Anesthesiology, Duke University Medical Center, Durham, NC, USA. OBJECTIVES: Loxosceles reclusa (brown recluse) spider bites can produce severe skin lesions that may necessitate extensive surgical repair. This study delineated the effects of hyperbaric oxygen (HBO2) therapy on these lesions by performing a prospective controlled animal study. METHODS: After approval by the Institutional Animal Care and Use Committee, 41 New Zealand white rabbits received 64 intradermal injections of 73 microL of raw venom extract mixed with physiologic buffered saline (Dulbecco's solution). Control injections were made with buffer. The animals were divided into 5 groups: 1) venom and no HBO2; 2) venom and 1 immediate HBO2 treatment (100% O2); 3) venom and immediate HBO2 with 10 treatments (100% O2); 4) venom and then delayed (48 hr) HBO2 therapy with 10 treatments (100% O2); and 5) venom and immediate hyperbaric treatment with normal inspired PO2 for 10 treatments (8.4% O2). Three animals in group 2 also received a control sodium citrate buffer injection. HBO2 treatments were at 2.5 atm absolute (ATA) for 90 minutes twice daily. Daily measurements were made of the lesion diameter, and skin blood flow using a laser Doppler probe. RESULTS: There was no significant effect of HBO2 on blood flow at the wound center or 1-2 cm from the wound center. Standard HBO2 significantly decreased wound diameter at 10 days ($p < 0.0001$; ANOVA), whereas hyperbaric treatment with normoxic gas had no effect. Histologic preparations from 2 animals in each group revealed that there were more polymorphonuclear leukocytes in the dermis of all the HBO2-treated animals when compared with the venom-alone and sodium-citrate controls. CONCLUSION: HBO2 treatment within 48 hours of a simulated bite from L. reclusa reduces skin necrosis and results in a significantly smaller wound in this model. The mechanism appears unrelated to augmented local blood flow between treatments.

Necrotizing soft tissue infections. Risk factors for mortality and strategies for management. Ann Surg 1996 Nov;224(5):672-683; Elliott DC, Kufera JA, Myers RA. Department of Surgery, R Adams Cowley Shock Trauma Center, Baltimore, Maryland, USA. OBJECTIVE: The authors evaluate in a retrospective fashion the factors influencing outcome in a large group of patients presenting with necrotizing soft tissue infections, thus propose a plan for optimal care of such patients. BACKGROUND: In many smaller series of patients with necrotizing soft tissue infections, similar analyses of risk factors for mortality have been performed, producing conflicting conclusions regarding optimal care. In particular, debate exists regarding the impact of concurrent physiologic derangements, type and extent of infection, and the role of hyperbaric oxygen in treatment. METHODS: A retrospective chart review of 198 consecutive patients with documented necrotizing soft tissue infections, treated at a single institution during an 8-year period, was conducted. Using a model for logistic regression analysis, characteristics of each patient and his/her clinical course were tested for impact on outcome. RESULTS: The mortality rate among the 198 patients was 25.3%. The most common sites of origin of infection were the perineum (Fournier's disease; 36% of cases) and the foot (in diabetics; 15.2%). By logistic regression analysis, risk factors for death included age, female gender, extent of infection, delay in first debridement, elevated serum creatinine level, elevated blood lactate level, and degree of organ system dysfunction at admission. Diabetes mellitus did not predispose patients to death, except in conjunction with renal dysfunction or peripheral vascular disease. Myonecrosis, noted in 41.4% of the patients who underwent surgery, did not influence mortality. CONCLUSIONS: Necrotizing soft tissue infections represent a group of highly lethal infections best treated by early and repeated extensive debridement and broad-spectrum antibiotics. Hyperbaric oxygen appears to offer the advantage of early wound closure. Certain markers predict those individuals at increased risk for multiple-organ failure and death and therefore assist in deciding allocation of intensive care resources. The impact of ischemia on wound healing is increased in old age but can be countered by hyperbaric oxygen therapy. Mech Ageing Dev 1996 Oct 25;91(2):131-144; Quirinia A, Viidik A. Department of Connective Tissue Biology, Institute of Anatomy, University of Aarhus, Denmark. The healing of normal incisional wounds and ischemic flap wounds was investigated in young (10 weeks) and old (102-104 weeks) rats, together with the effect of treatment with hyperbaric oxygen on day 0-3 of healing. After 10 days of healing all biomechanical strength parameters of normal wounds were decreased by 30-40% and of ischemic wounds by 40-51% in the old animals compared with the young controls. After 20 days all strength parameters of normal wounds and ischemic wounds were decreased by 29-37% and 46-58%, respectively, in the old rats compared with those of the young ones. Treatment with hyperbaric oxygen of ischemic wounds in old animals increased all strength parameters by 36-50% after 10 days and by 67-88% after 20 days. For young animals, the corresponding increase was only 21-35% after 10 days and no effect was seen after 20 days. The shrinkage of ischemic wounds was decreased by 48% in the old animals compared with the young ones. It can be concluded that ischemia intensifies the impairment of the healing seen in old age. On the other hand, treatment of ischemia with hyperbaric oxygen is much more effective in old animals, despite the fact that it also has a pronounced effect in young animals. Furthermore, the results suggest a decreased wound contraction with age.

Iatrogenic air embolism. Presse Med 1996 Oct 19;25(31):1466-1472; Bacha S, Annane D, Gajdos P Service de Reanimation medicale, Hopital Raymond-Poincare, Faculte de Medecine de Paris-Ouest, Garches. The incidence of iatrogenic (physician created) air embolism can only be estimated since many accidents are not recognized. Clinical manifestations, essentially neurological or cardiovascular disorders vary greatly. Air embolism may occur during coronary or cerebral arteriography, cardiopulmonary bypass, venous catheterism, various types of surgery or blood transfusion among other situations. Once air has entered the arterial circulation, the bubble of gas follows the blood flow until it is blocked by a smaller calibre vessel. The progressive diffusion of the air reduces the size of the embolus which then migrates on to smaller and smaller vessels. Subsequent pathological manifestations of air embolism result from mechanical obstruction leading to ischemia and inflammatory reactions to air acting as a foreign body. The sudden onset signs of neurological impairment with or without a cardiopulmonary component in patients in a high-risk situation leads to clinical diagnosis. Treatment must be started immediately although brain CT scan or echocardiography may help confirm the diagnosis. The source of the air must be immediately identified and removed and the vital functions controlled. Mechanical or facial mask ventilation with pure oxygen is indicated. Hyperbaric oxygen therapy should be instituted. Morbidity and mortality after iatrogenic air embolism is high but major improvements have been achieved with oxygen therapy. Neurological sequellae have been estimated to reach 19 to 50% of the patients. A personal controlled prospective study revealed 14% mortality after hyperbaric oxygen therapy given within 12 hours of the accident. [It would be better to get in a chamber at the first sign of trouble.]

The hyperbaric oxygen therapy of disordered ammonia detoxication in the operated liver. Anesteziol Reanimatol 1996 Sep;5:64-67; Savilov PN. The status of the main routes of ammonium detoxication in the liver (synthesis of glutamine and urea) after its resection and hyperbaric oxygenation (HBO2) was studied in 160 rats. HBO2 (3 sessions at 3 atm. abs.--50 min) following resection of the liver stimulated the activity of glutamine synthase and prevented the reduction of glutamate (a substrate for glutamine synthesis) level in the operated on liver. Hyperbaric oxygen activated the glutamine-dependent and non-glutamine-dependent pathways of urea synthesis in the resected liver and ensured the incorporation of glutamine amido groups in the ornithine cycle. HBO2 boosted the inhibitory effect of liver resection on the activity of glutamate dehydrogenase and prevented the accumulation of ammonium in the hepatocytes of resected liver. The stimulating effect of HBO2 on the ammonium-detoxifying function of the resected liver persisted for 11 days after the exposure. [HBO2 is good for sick livers!]

Actinomycosis. Ann Otolaryngol Chir Cervicofac 1996;113(5):289-93 [Mucormycosis-actinomycosis and caseous dental sinusitis associated with sinusal foreign body]. Braun JJ, Gentine A, Bourjat P, Koenig H, Conraux C Service ORL, Hopital de Hautepierre, Strasbourg. The authors report an uncommon case of caseous dental sinusitis with infection or superinfection by mocorales and actinomycetes. The patient was healthy, without diabetes mellitus, but was treated for lymphoma 18 years before. This observation leads to a discussion of nosologic, diagnostic and therapeutic features of caseous sinusitis, dental or not, fungal or not, which are often or too often called aspergillosis sinusitis. The recovery of the patient was complete after surgery, amphotericin B and hyperbaric oxygen. Ref: Stomatologiia (Mosk) 1980 Mar-Apr;59(2):28-9 [Use of hyperbaric oxygenation in the

therapy of maxillofacial actinomycosis]. Bazhanov NN, Kasparova BV, Kapnik VI, Genkin ME, Novikova L. JAMA 1969 Oct 20;210(3):552-3 Hyperbaric oxygen in the treatment of actinomycosis. Manheim SD, Voleti C, Ludwig A, Jacobson JH 2d

Q: Would you use HBO2 to treat a 73 year old alcoholic who fell causing head trauma and broken bones? He is disoriented and may have muscle necrosis. A: Yes and here are some reasons: Edema limits oxygen transport from poor solubility of oxygen in water. Oxygen under hyperbaric conditions corrects edema by reducing blood flow and reduces tissue hydrostatic pressure allowing better lymphatic drainage. Fracture, when a bone is broken the blood supply is damaged and oxygen transport is reduced. Healing is oxygen dependent and the rate of bone formation even in uncomplicated fractures improves with intermittent high dosage oxygen. Soft tissue damage, the rate of collagen formation and the tensile strength are doubled under hyperoxic conditions. The cerebral effects may be due to fat embolism which responds well to hyperbaric oxygenation. Philip Cohen Professor of Biochemistry at the University of Dundee lectured today on the central role of the phosphorylation of proteins in health and disease and the problems associated with abnormal phosphorylation. Of about 30,000 proteins present in the body 1 in 3 are phosphorylated and this is facilitated by protein specific kinases. All kinases use only ATP as the substrate for protein phosphorylation. This is one key piece in the jigsaw to allow us to understand why hypoxia, which is not severe enough to cause actual membrane pump failure, is so damaging and why a modest elevation of oxygen delivery such as 1 hour in 24 hours of HBO2 is so effective. - Philip James, Wolfson Hyperbaric Medicine Unit, University of Dundee, Ninewells Medical School

HBO2 IN MONOXIDE POISONING: A 10 YEARS' EXPERIENCE AT A T.I.P. HYPERBARIC MEDICAL CENTRE IN PADUA (ITALY); 719 CASES ARE UNDER EXAMINATION. Vincenzo Zanon1, Fabrizio Rusca2, Giacomo Garetto1, Rocco Scappatura1 & Giampiero Giron1. 1A.T.I.P., Unit of Hyperbaric Medicine, Institute of Anesthesia and Reanimation & 2Institute of Anesthesia and Reanimation, Faculty of Medicine, University of Padua, Padua, Italy INTRODUCTION: From March 6th 1985 to March 31st 1995 we treated 719 cases suffering from acute monoxide poisoning with hyperbaric oxygen therapy, at an average of approximately 60 cases/year. In the 16 month period from January 1st 1993 to May 24th 1994 we treated more than half of the total cases of the previous seven years. METHODS: Hyperbaric oxygen (HBO2) treatments were conducted at 2.8 ATA for 75 min, for all cases where at least one of the following criteria were met: 1) anamnestical proof of toxic exposure. 2) COHb-aemia >25%; 3) significant neurological and/or cardiac clinical conditions. RESULTS: With a single (HBO2) treatment (2.8 ATA or 18m: 25 min. of 100% O2+ 5 min. air break + 25 min. of 100% O2 + 5min. air break + 25 min. of 100% O2) we did not observe any symptoms of O2 toxicity and, as per neurological sequelae, our results are within bounds previously reported: 0.03% Schillito (1963), 1% Kuroiwa (1967), 1.52% our report (A.T.I.P. - 1995), 10% Richardson (1959). CONCLUSIONS: HBO2 continues to prove itself as being the basic therapy for acute CO poisoning, provided we resist the temptation of correcting its moderate acidosis.

Carbon monoxide: The key issue with carbon monoxide - as it is generally with HBO2 - is the timing of the intervention. Initially CO produces acute hypoxia, but this is rapidly accompanied by the development of cerebral edema because of failure of the blood-brain

barrier - cf bubble disease. Edema limits oxygen transport - as oxygen is poorly soluble in water leading to a vicious cycle. As the condition progresses the correction of the failure of oxygen delivery becomes impossible even under hyperbaric conditions. This can be seen in head injury where each HBO2 session reduces intracranial pressure and in the interval it rises again. If the oxygen is able to restore the Blood Brain Barrier then the process comes under control. (Reference Sukoff MH and Ragatz RE. Hyperbaric oxygenation for the treatment of acute cerebral edema. Neurosurgery 1982;10:29-38.) The standard method for detecting CO in mines was a biological monitor - a canary in a box. JS Haldane devised a "humane apparatus" in which an oxygen cylinder formed the handle. When the bird fell off the perch the oxygen was switched on to revive it and so the same bird could be used many times. Haldane also demonstrated that oxygen protects against CO - 1.8 atmopsheres protects against 1 atm of CO - an experiment conducted in a chamber. I do not know of any toxicity of CO which is not related to the production of hypoxia - but as CO is highly reactive chemically it is possible but the above experiment suggests it is unlikely. However blockage of the cytochrome enzymes is so fundamental to life that other factors are likely to be unimportant. In survivors of acute CO poisoning as with other insatnces of survival from hypoxia - such as the inhalation of say pure helium or nitrogen - when the patient survives with brain damage other organ systems appear to be intact. For example, they do not develop acute hepatic or renal failure. The pattern of brain damage in CO poisoning is the same as in anoxic asphyxia where the brain is perfused with blood without oxygen. (Reference James PB, Calder IM. Anoxic asphyxia - a cause of industrial fatalities: a review. JRSM 1991;84:493-495. This is because the nutrition of the white matter and the basal ganglia is largely dependent on the draining veins which are surrounded by capillary free zones. (Reference Pfeifer RA. Grundlegender untersuchungen fur die angio-architektonik des menschlichen gehirns. Berlin Springer, 1930.) By the way apoptotic programming of cell death appears from the latest evidence to be reversible. The consequences of failure to use oxygen properly are horrendous for patients and their relatives. Such patients can now survive for years in vegetative states. The cost of the care of only one such patient would pay for many chambers. I agree with the statement that every emergency room should have a chamber especially those at altitude! Philip

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SEQUELAE- SHORT FOLLOW-UP PERIOD. 5. Raphael JC et al. Trial of normobaric and hyperbaric oxygen for acute carbon monoxide intoxication. Lancet 1989; Aug 19:414-418. UNBLINDED RCT. NO EVIDENCE OF SIGNIFICANT BENEFIT OF HBO. Patients are dying every day because the vast majority of physicians regard hemoglobin saturation as the correct end point for oxygen administration. The problem we face in establishing the correct dosage of oxygen for acute conditions is the same as that faced for most acute interventions - the very variable nature of the patient's condition, the timing and the fact that it is difficult in an acute life-threatening situation to introduce scientific methods and objectivity. A similar controversy has surrounded the use of IV fluids and I suspect that we would not be having this discussion if the provision of high dosages of oxygen was as easy as administering IV fluids. The drive to produce a fixed protocol for the use of hyperbaric oxygen therapy is absurd because of these variables. The practice of medicine has to be undertaken intelligently - if the cookbook approach is adopted then clinical training is unnecessary. The only objective measurement we have of CO is of course the carboxyhaemoglobin level. The half life of COHb is about 5.5 hours breathing air, 1.75 hours breathing oxygen at sea level and about 20 minutes breathing 100% oxygen at 3 atm abs. The COHb level is not a guide to treatment because patients can remain in coma when the COHb level is unmeasurable. This is because CO poisons the active transport mechanisms responsible for the blood-brain barrier and in an animal model the administration of 2000 ppm CO causes brain herniation through the trephined skull. The barrier disturbance was followed by Tracy Putnam in the mid 1930's using fluorescin in the cat. I am surprised at your rejection of animal evidence. Oxidative metabolism is much the same in other animals although dogs apparently do not produce catalase. The presence of hypoxia in tissue can be demonstrated by MRS and I look forward to the day - although I may not live to see it - when we can adjust the oxygen dosage on the basis of real time data. Our tolerance to hypoxia is poor and the induction of unconsciousness by hypoxia is very reproducible. Equally the reversal of the effects I equally reproducible provided the additional oxygen is provided promptly. Unfortunately the Kleijen review was confined to short term trials that included patients with advanced disease. Only long-term controlled studies have shown persistent benefit of HBO for MS. A very recent publication has endorsed their findings and concludes that HBO treatment should be instigated as soon as the condition is diagnosed and before irreversible lesions have become established. - Treatment of Multiple Sclerosis with Prolonged courses of Hyperbaric Oxygen: A 13 year Update - Perrins D.J.D. & James P.B. In Proc. 12th International Congress on Hyperbaric Med. Sept 1996, Best Publishing Company. Carbon monoxide is very reactive and not only readily binds to haemoglobin it also binds to other metallo proteins such as the cytochrome enzymes - in other words it is - to quote Haldane - a tissue poison. It is this latter mechanism which is the problem, not the relative anaemia caused by the loss of haemoglobin transport. Goldbaum et al removed blood from dogs exposing it to CO outside the body. When retransfused they achieved a carboxyhaemoglobin level of 60-70% which if it is achieved by allowing the animal to breathe some CO is always fatal. The plasma borne CO is able to poison endothelial mechanisms and alter characteristics of blood elements such as leucocytes altering their adhesion and causing obstruction to blood flow and free radical damage. Because the blood brain barrier is energy dependent it fails, becoming very permeable. The resulting edema causes an increase in intracranial pressure reducing blood flow and oxygenation. In patients who recover, the mid brain areas - basal ganglia - are the most damaged because of the dependence of many areas on venous blood

for their oxygenation. A wide variety of syndromes may result from spastic cerebral palsy to personality disorders and even short-term memory changes. Because the changes can occur quickly it is essential to treat this as an absolute emergency - compare this to anoxia caused by cardiac arrest where we try to restart the heart as quickly as possible. Every hospital should have at least a monoplace chamber. Philip James, Wolfson Hyperbaric Medicine Unit University of Dundee Reference: Goldbaum LR, Ramirez RG, Absalon KB. Joint Committee on Aviation Pathology. 13. What is the mechanism of carbon monoxide toxicity? Aviat Space Environ Med 1975 46 1289-129.

Half Life for COHb about 5hrs 25min when breathing air at 1 ata

Half Life for COHb about 1 hr 26 min when breathing 100% O2 at 1 ata

Half Life for COHb about 23 min when breathing 100% O2 at 2.8 ata

HBO2 AS ADJUNCT THERAPY IN THE TREATMENT OF FROSTBITE: A PROGRESS REPORT. F. BajroviÊ1, M.J. Tipton2, F.S.C. Golden2 & I.B. Mekjavic3. 1Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana; 2University of Surrey / Insitute of Naval Medicine, United Kingdom & 3Department of Automatics, Biocybernetics & Robotics, Joæef Stefan Institute, Ljubljana, Slovenia.
INTRODUCTION: Following initial treatment of frostbite of an extremity by rewarming, to prevent direct injury from intracellular ice formation and protein denaturation, medical treatment is directed toward prevention of additional injury and abrogation of affected ischemic tissue due to microvascular damage. Though several case studies have been reported, whereby HBO2 was successfully applied in the treatment of frostbite injury, it is not normally included as an adjunct to conventional treatment. To date, we have been requested to provide HBO2 therapy in a total five frostbite cases. METHODS: A total of five patients with frostbite injury have been referred to our laboratory for HBO2 therapy. With the exception of one patient, all recieved treatment within several days of the injury. One patient recieved the injury in the Himalayas, and there was a several week delay between injury and the first treatment. The patients were treated at 2.5 ATA for 90 minutes, some reciveing two treatments daily and others only one treatment daily. The number of treatments varied among patients, from 14 to 30. RESULTS: In patients recieving HBO2 therapy within days of injury, the injury healed. CONCLUSIONS: It is concluded that HBO2 therapy should be considered as an adjunct therapy in the treatment of frostbite. This work was supported by the Ministry of Science and Technology (Slovenia).

HOW MANY HBO2 TREATMENTS ARE NECCESSARY FOR THE THERAPY OF SUDDEN DEAFNESS AND ACUTE TINNITUS? W. Welslau1, A. Lammerding2, M. Almeling1, R. Busch1, G. Trombitas1 & G. Hesse3. 1Druckkammerzentrum, Hansteinstr. 29, 34121 Kassel, Germany; 2Druckkammerzentrum, 34454 Bad Arolsen, Germany & 3Tinnitus Klinik, Große Allee 3, 34454 Bad Arolsen, Germany. INTRODUCTION: Since the 1st ECHM conference (1994) sudden deafness is an accepted HBO2 indication. The aim of this study was to evaluate HBO2 effectiveness in sudden deafness/acute tinnitus according to number of treatments (10/15). METHODS: Patients with sudden deafness and acute tinnitus were treated with HBO2 after standard treatment (i.v. infusions, rheological drugs) without sufficient improvement. Prior to HBO2 therapy, after 10 and 15 treatments, and at least 3 months later, we took a tone audiogram and/or a questionaire with a visual

analogue scale (VAS) according to recommendations of the 4th International Tinnitus Seminar, Bordeaux (´91) to determine tinnitus loudness. In the tone audiogram, a threshold recovery in 2 frequencies of over 10 dB and up to 20 dB was regarded as improvement, and over 20 dB as good improvement. In VAS we regarded 50% or less of initial loudness as improvement. Patients were treated 15 times on six days/week, breathing 100% oxygen for 60 min. at 250 kPa. RESULTS: From January to June 1996 we treated 129 patients. Mean delay after onset of symptoms was 6 weeks. In patients with sudden deafness (n=43) improvement in hearing was achieved in 11 patients (25.6%) after the 10th treatment and 14 patients (32.6%) after the 15th HBO2 session. Follow up at >3 months after HBO2 showed similar results (13 patients). Acute tinnitus loudness was found to decrease by < 50% in 10.9% of the patients after 10 treatments, and in 45.0% of the patients after 15 treatments (n=129). In the follow up, these results were kept within 39.8% (n=123). CONCLUSIONS: In sudden deafness and tinnitus 15 HBO2-treatments show better results than 10 treatments. These results are confirmed by a follow up 3 months after HBO2.

Hyperbaric oxygen helps wound healing. REFERENCES: 1. Shweiki D. et al. (1992). Vascular endothelial growth factor induced by hypoxia may mediate hypoxia-initiated angiogenesis. Nature 359: 843 - 845. 2. Passaniti A. et al. (1992). A simple, quantitative method for assessing angiogenesis and antiangiogenic agents using reconstituted basement membrane, heparin, and fibroblast growth factor. Lab. Invest. 67: 519 - 528. 3. Knighton D. et al. (1983). Oxygen tension regulates the expression of angiogenesis factor by macrophages. Science 221: 1283 - 1289. 4. Knighton D. et al. (1981). Regulation of wound healing angiogenesis: Effect of oxygen gradients and inspired oxygen concentration. Surgery 90: 262 - 270. 5. Silver I. (1984). Cellular microenvironment in healing and non-healing wounds. In: Soft and Hard Tissue Repair. T.K. Hunt et al. (Eds.) New York: Praeger, pp. 50 - 66. 6. Knighton D. et al. (1984). Regulation of repair: Hypoxic control of macrophage mediated angiogenesis. In: Soft and Hard Tissue Repair. T.K. Hunt et al. (Eds.) New York: Praeger, pp. 41 - 49. 7. Hammarlund C. (1994). The physiologic effect of hyperbaric oxygen. In: Hyperbaric Medicine Practice. E.P. Kindwall (Ed.) Flagstaff, Arizona: Best Publishing Co., pp. 17 - 32. 8. In the Annals of the Royal College of Surgeons of England Vol.61, 1979 Dr. Loder reported on 71 cases, over a 7 year period. The patients with bad wounds received pure oxygen at 2.5 atmospheres absolute pressure for one hour, three times per day to start. As improvement occurred the frequency went to once per day until the wound completely healed. The author wrote that he was surprised how often the doubtful limb or skin area survived. 9. Doctor I. Eltorai wrote a comprehensive reports to chronicle the use of hyperbaric oxygen for wound healing. Reference: Hyperbaric Oxygen in the Management of Pressure Sores in Patients with Injuries to the Spinal Cord Journal Dermatol. Surg. Oncol. 7:9 Sept 1981. Extensive literature summaries of 34 references highlighted the great results achieved with hyperbaric oxygenation for wound healing. The last portion of the manuscript listed the doctor's hospital practice results at the Spinal Cord Injury Center of the Long Beach Veterans Administration Hospital. Some noteworthy findings included: Fastest healing of open, full thickness wounds occurred during continuous exposure to a concentration of oxygen of 45% and slowest at concentrations less than that of air. Intermittent exposure to hyperbaric oxygen improved healing of skin wounds to various depths. Occlusive dressings upon wounds, that excluded oxygen, retarded skin healing. Hyperbaric oxygen at 2 atmospheres not only prevents skin flap death, but also enhances blood vessel regrowth into skin grafts.

Moderate increased oxygen increases the rate of skin growth and repair. Collagen synthesis, necessary for deep wounds, often inhibited in serious wounds with damaged blood circulation, increased in hyperbaric oxygen with a peak of 70% oxygen. Bacteria infection in wounds reduces the available oxygen and thus impairs collagen production. Hyperbaric oxygen inhibits gram-positive, gram-negative, and anaerobe bacteria in wounds thereby increasing available oxygen and promoting collagen synthesis for successful wound repair. Hyperbaric oxygen stimulates bone growth cells and bone resorption cells thus improving bones' ability to clear debris and repair itself.

National Institute of Health Consensus Report: Osteoradionecrosis (ORN), a relatively uncommon clinical event, is a consequence of hypovascularity, the cytotoxic effects of radiation on bone-forming cells and tissue, and is associated with hypoxia of the affected bone. As a consequence, when bone is injured, it is unable to heal and becomes susceptible to secondary infection. This process can progress to pathologic fracture, infection of the surrounding soft tissues, and oral-cutaneous fistula formation. It is characterized by severe, constant pain. The risk of developing ORN is lifelong. Chemotherapy does not increase the risk of ORN. The initiating injury resulting in ORN is frequently the extraction of a tooth from an irradiated mandible. For this reason, all teeth that might have to be removed should be extracted before starting radiation therapy. If clinical conditions permit, at least 2 weeks, and ideally 3 weeks, should be allowed for adequate healing between the extraction and the commencement of radiation therapy. Healthy teeth should be preserved. Dentures causing ulceration of the atrophic mucosa over the mandible can initiate ORN. Spontaneous ORN can also occur without any obvious injury to the irradiated mandible. Traditional treatment of ORN with antibiotics and surgical debridement frequently fails with progressive involvement of the remaining mandible. The keystone of the treatment of ORN is the provision of adequate tissue oxygenation in the damaged bone. This is best done by using hyperbaric oxygen therapy (HBO2). Multiple treatments are required. Early stages of ORN without fracture or fistulae may be cured by HBO alone. More advanced cases, in addition to HBO, require sequestrectomy or partial mandibulectomy with eventual bone grafting.
Reference: Undersea Hyperb Med 1997 Jun;24(2):117-22

Q: Are their protective mechanisms in the body to prevent excessive oxygenation? A: If resistances in the pathway from lung to the mitochondria of a particular tissue cause the final oxygen tension at mitochondrial level to fall then hyperbaric conditions are necessary to establish normal oxygenation. During hyperbaric oxygenation autoregulation reduces oxygen levels to near normal values, with the exception of the lung and endothelial tissues of the pulmonary venous vessels, the heart and the arterial tree. Tensions in the CNS (canine) indicate that autoregulation reduces oxygen levels to nearly normal values over about 30 minutes even from 3 atm abs. in normal tissue.

Pathophysiological mechanisms of tissue hypoxia: Arterial hypoxaemia, Low inspired oxygen partial pressure (high altitude), Alveolar hypoventilation (sleep apnoea, opiate overdosage), Ventilation-perfusion mismatch (acute asthma, atelectasis), Right to left shunts, Failure of oxygen-haemoglobin transport system, Inadequate tissue perfusion, Low haemoglobin concentration, Abnormal oxygen dissociation curve (haemoglobinopathies, CoHb), Histotoxic poisoning of intracellular enzymes (cyanide, septicaemia) Note that they have not included: Vessel wall changes and edema which limit transport to tissue. To

ensure adequate tissue oxygenation should be the FIRST objective of therapy in medical practice. The on going debate on the list about "HBO2" repeats arguments that have been aired many times. The phrase "hyperbaric oxygen" is grammatically incorrect. The correct term is oxygenation. We should simply refer to "oxygen therapy." It is clear that many - perhaps the majority of physicians actually involved in the provision of oxygen under hyperbaric conditions as a therapy do not see it as a continuation of the use of additional oxygen provided without a chamber. Hence "hyperbaric" oxygen has to be proven whereas "normobaric" oxygen does not. Let us not doubt that the oxygen provided under hyperbaric conditions WORKS. Why? Because when a patient breathes this oxygen it is providing the oxygen that the patient would require during that time from breathing air. The same argument applies to the use of IV fluids which can provide the water that a patient would otherwise have to drink. The issue that has to be addressed is - Is the ADDITIONAL oxygen actually beneficial - that is - can it correct a pathological situation in addition to providing the substrate for metabolism. I submit that the evidence that oxygen is capable of being involved in this way is beyond dispute. If we measure tissue hypoxia then we have a duty to correct it. Oxygen is transported across the alveolar membrane and enters plasma. Some is then taken up by haemoglobin and some remains in plasma. Under normal conditions - that is at a standard atmosphere which is defined as 1013 hPa or 760 mm Hg - 100 ml of arterial blood carries about 19 ml of oxygen as oxyhaemoglobin and only 0.3 ml in solution. Hence the latter is often ignored. However only the oxygen in the plasma is available for transport through the capillary wall into the tissues and the concentration or tension determines the rate.Oxygen has to dissociate from haemoglobin to be available. The plasma oxygen tension breathing air with oxygen at a partial pressure (Dalton's Law) of 2 tenths of an atmosphere (21% of 1 atm abs) is about 95 mm Hg. Increasing the oxygen inspired to 100% multiplies the amount in solution by a factor of 5 - hence (Henrys Law) the amount carried in solution is multiplied by five to 1.5 ml at 3 atm abs it is 4.5 ml per 100 ml blood which is the normal arterial - venous difference at rest. Hence all the requirements of the body can be met by the oxygen in the plasma. However the gradient is what is so important in therapy - over 2000 mm Hg can be achieved - a more than twenty fold increase. As a consequence life can be supported with blood for a short time and the paper was published in 1959. Used properly oxygen is the most powerful therapeutic tool in medicine. We need to ensue our medical students are taught properly but after 25 years in this school we have only just established oxygen therapy in the curriculum. Philip James

Philip James writing about safety issues: We have operated chambers limited to 2 atm abs with trained volunteers for 17 years without a patient incident - in excess of 1.3 million hours. Ironically I predicted that a drench system would be used by mistake when the Health and Safety Inspectorate insisted on them here. Eventually they will kill someone - as the result of a heart attack with gallons of cold water cascading on the patient. This is a similar situation to air bags in cars. The principle is KISS - keep it simple stupid ! The most irresponsible use of hyperbaric chambers is in aviation - letting pressure vessels leave the ground. The growth of the parental interest in the treatment of children is the most important event in the history of hyperbaric oxygen therapy because it highlights that more oxygen should be used to prevent such brain damage at the appropriate time. Parents become aware. Dr C Sanchez gave a stunning presentation on using HBO2 in the neonate at the recent seminar in Columbia South Carolina. His slides on infants with necrotising fasciitis were astounding. I was fortunate enough to be be given a certificate stating that I

have successfully attended a 15 hour course in hyperbaric medicine signed by a CHT - a great relief after 27 years in the business. Philip James

The UHMS has accepted a new indication for HBO2 after years in which the number of indications has steadily declined. It is a neurological indication which is a first - no other neurological indications are accepted with the exceptions of air embolism and decompression sickness...It is cerebral abscess. Is this indication supported by double-blind controlled trials? No, just a few cases. Philip James, Wolfson Hyperbaric Medicine Unit, University of Dundee Dr Andel wrote: Cerebral abscess indication was accepted because in a HBO2 group of 18 patients with manifest severe intracerebral absesses no patient died (whereas with "conventional" approach including high tech ICU the lethality worldwide is well above 70% - beside this, basline work with animal-models has been conducted - showing clearly the pathomechanism all patients have been well documented including CT ! Dr. James wrote in reply: Thank you for the information on cerebral abscess. As I said a few cases just life versus death - and you are unable to support the treatment of carbon monoxide poisoning ! It is of course fully supportable by such evidence. The Lancet has published a paper from Amsterdam on the successful treatment of haemorrhagic cystitis with hyperbaric oxygen therapy. It is untreatable in any other way and this was clearly recognised by the reviewers for the Lancet, but the UHMS have not included it. It is no help to be so inconsistent. The profession is beginning to wake up to the fact that patients are dying because of lack of oxygen. This letter is from the British Medical Journal 27 March 1999. Best wishes to all - Philip James Fear of hypercapnia is leading to inadequate oxygen treatment Editor - Patients with proved hypoxaemia who are receiving a fractional inspired oxygen concentration of only 24-35% can be found in Wards throughout the United Kingdom. Even this is overstating the case since masks often do not deliver the set oxygen concentration, and an ill fitting facemask with a resultant increase in entrained room air will further reduce the inspired oxygen concentration. 1,2 I was therefore delighted by Bateman and Leach's statement that 'Inadequate oxygen accounts for more deaths than can be justified by the relatively small risks associated with high dose oxygen." It was disappointing then to find that most of the article dealt with oxygen delivery systems designed to deliver a low percentage of oxygen. It was also frustrating to read a recommendation that the maximum permissible inspired oxygen concentration is 60% in a non-arrested hvpox-aemic patient. A subsequent article in the ABC of Oxygen again stated that 24-28 oxygen should be used tor patients with chronic obstructive airways disease until arterial gas analysis is available because of the possibility of hypercapnia 5 This fear has been successfully transmitted to generations of medical students, who have subsequently been unable to bring themselves to adequately treat documented hypoxemia. In intensive care respiratory depression can be treated by instituting or increasing mechanical ventilation, a treatment not immediately available to most respiratory physicians. Over 15 years, I have seen a small number of patients who exhibited moderate and gradual rises in partial pressure of carbon dioxide because of loss of hypoxic drive. In no case did the hypercapnia constitute a risk to life or an acute emergencies. Hypoxaemia, however, is responsible for many cardiorespiratory arrests and does represent a sudden and profound risk to life. The standard thinking on oxygen therapy and chronic lung disease requires a change in emphasis. We should highlight statements such as that with which Bateman and Leach finish their article: "Failure to correct hypoxemia for fear of causing hypoventilation and carbon dioxide retention is unacceptable clinical practice." G Lavery Intensive care

consultant Regional Intensive Care Unit. Royal Hospitals Trust. Belfast Goldstein RS. Young J, Rebuck AS. Effect of breathing pattern on oxygen concentration received from standard face masks Lancet 1982; ii: 1188 -90. Cox C. Gilbe C. Fixed performance oxygen masks. Hypoxic hazard of low-capacity drugs. Anaesthesia 1981;36:958-964 Hunter J Olson LC. Performance of the Hudson multi-vent oxygen mask Med J Aust 1988;148:444-7. Bateman NT Leach RM. Acute oxygen therapy. BMJ 1998:317 798 (19 September). Rees PJ Dudley Oxygen therapy in chronic lung disease. BMJ 1988;317:871-4 (26 September).

Hyperbaric oxygen therapy of carbon monoxide poisoning: I suggest that the finding by Scheinkestel (1) that the outcome of the treatment of patients poisoned with carbon monoxide using additional oxygen under hyperbaric conditions was worse than using 100% oxygen at normal atmospheric pressure was because of oxygen toxicity. A very high dosage of oxygen was used and so one poison was substituted for another. The dosage of oxygen is just as important as with a pharmaceutical and more is not always better. As Paracelsus stated, all substances are toxic only the dose makes the thing not a poison. Oxygen is significantly toxic when given at 2.8 atm abs for an hour and is normally used at this pressure for a maximum of 20 minutes. This derives from US Naval practice (2) in the treatment of gas bubble disease. The use of 2.8 atm abs breathing oxygen was a compromise between the use of pressure to reduce the gas volume and the risk of convulsions from oxygen toxicity. The risk of convulsion becomes substantial if the time breathing oxygen at this pressure extends to 30 minutes. (3) For example, a 19 year old candidate for diver training became nauseated after 27 minutes breathing oxygen at 2.8 atm abs and despite the mask being removed had a grande mal convulsion. However, a seizure is an overt manifestation of toxicity and the earliest biochemical markers of toxicity can be detected as low as 1.75 atm abs. (4) Kelly (5) using electrodes to measure oxygen levels in the CNS, demonstrated that the administration of pure oxygen causes vasoconstriction reducing blood flow, which returns tissue oxygen levels to normal in about 20 minutes. This provides strong support for the adoption of this duration by the US Navy. However, this autoregulation may be lost as the partial pressure is increased beyond 2 atm abs, where vasodilatation or severe vasoconstriction may occur. Soon after the introduction of the oxygen tables in the treatment of gas bubble disease by the US Navy worsening of symptoms was observed breathing oxygen at 2.8 atm abs and this is stated in the first US Navy manual to incorporate these procedures published in 1970.2 This worsening cannot be because of an increase in nitrogen content, or bubble size, and this also points to oxygen toxicity as the cause. In 1895 Haldane6 demonstrated that hyperbaric oxygenation can actually prevent the toxicity of a lethal level of carbon monoxide. Clearly timing is important and the mean delay to treatment in the [questionable] study was over 7 hours, by this time the level of carbon monoxide is low and it is the sequelae that are being treated. They are associated with blood brain barrier disturbance and cerebral oedema. This trial certainly does not invalidate the years of experience in reversing the toxicity of carbon monoxide using the appropriate dosage of oxygen under hyperbaric conditions. It also illustrates that those with little experience in a field should consult widely before planning studies. Philip James MB ChB, DIH, PhD, FFOM References: 1. Scheinkestel CD, Bailey M, Myles PS, et al. Hyperbaric or normobaric oxygen for acute carbon monoxide poisoning; a randomised controlled clinical trial. Med J Aust 1999;170:203-210. 2. US Navy diving manual 1970, Navships 0994-001-9010 Navy Department, Washington. 3.

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Dr Cuau Sanchez in Mexico is pioneering the use of hyperbaric oxygenation in neonatal encephalopathy and necrotising fasciitis. He presented this paper at the meeting in Columbia South Carolina 9th April. The abstract that follows sets the scene - hypoxia detected by the presence of lactate magnetic resonance spectroscopy in the neonate. Lactate is produced by anaerobic metabolism - because there is not suficient oxygen. Reading about the improvements in children such as Ian and Micah produced so long after the event indicates how dramatic the improvement would be if sufficient oxygen was used at the appropriate time. Best wishes, Philip James, Wolfson Hyperbaric Medicine Unit, University of Dundee

HYPERBARIC OXYGEN THERAPY IN NEONATES E. Cuauhtimoc Sanchez R., M.D. Medical Director Servicio do Medicina Hiperbarica Hospital Angeles del Pedregal Mexico, D.F. Introduction: The use of Hyperbaric Oxygen Therapy (HBO2) is extensive in adults and is becoming more common in the pediatric patient. Nevertheless, there is great reluctance to treat neonates in hyperbaric chambers. The use of HBO2 in pediatric patients was relative common in the former USSR and by 1981 there were reports of over 1868 cases treated. However, there are very few reports of neonates being treated with HBO2 and most of them date from the 60's. We have started treating neonates in our monoplace chambers (Sechrist Series 3200) for the following conditions: acute severe intestinal ischemia, necrotizing enterocolitis, and acute ischemic/anoxic encephalopathy. Severe Intestinal Ischemia and Necrotizing Enterocolitis There are reports on the use of HBO2 in relation to intestinal pathologies, such as, radiation necrosis, intestinal pneumatosis, intestinal ischemia, intestinal ischemia/reperfusion injury, intestinal obstruction, Crohn's disease, systemic inflammatory response, bacteria translocation, intestinal sepsis, and necrotizirig enterocolitis. All of these reports support the use of HBO2. Hyperbaric oxygen therapy is not only useful for the intestinal pathology, but also for the systemic effects of which include disseminated intravascular coagulation (DIC), the systemic inflammatory response (SIR) and shock. Normally, neonates who are treated in the first 6 hours, respond in the first one or two treatments. It is rare for these patients to need more than 2 treatment, and it is only in those cases where there are surgical complications that further treatments may be required. The effects of HBO2 in neonates are visible within the first minutes post-treatment. In infants with severe intestinal ischemia and necrotizing enterocolitis there is a significant reduction of abdominal circumference, gut edema and pneumatosis. They also have stabilization of the systemic responses (DIC, SIR and shock). Oral feeding is usually restored in the first 24-h post-HBO2. Ischemic/Anoxic Encephalopathy: Again, the reported experience of neonates with this condition dates from the 60's and is mainly from the former USSR. The rationale for the use of HBO2 for this condition is to prevent the development of the primary ischemic/anoxic lesion and secondary ischemic/reperfusion

injury. We recommend treating these patients in the first 6 hours post-delivery. Our patients were studied with EEG and transfontanellar ultrasound to determine a baseline. All of the patients were re-studied 4-6 hours after HBO2 and there was no evidence of cerebral edema after the first treatment. A neonatologist and neurologist have been performing the follow-up and all patients have had adequate psychomotor development according to their age. There were no side effects in this group of patients, one with history of being premature with a hyaline membrane was treated preventively with inhaled surfactant and did not developed pulmonary oxygen toxicity. All the neonates were studied pre and post-treatment by fundascopic examination to rule out retinopathy of the premature. We have studied them every month, and so far there has been no evidence of it in our patients. Oxygen Toxicity: The lack of information about oxygen toxicity in neonates has hindered the development of HBO2 in these patients. According to the established milestones for ocular development, the distal third of the vasculature will develop up to the 34 th week of pregnancy. The retinopathy of the premature is generally due to breathing sustained high percentage of oxygen (above 45%) for long periods in incubators. Presently, the retinopathy of the premature is considered to be like an ischemia/reperfusion injury. HBO2 has been used to manage, and to prevent ischemia/reperfusion injury. Also, short exposures to low pressures (2.0 atmosphere absolute or 202kPa for 45 minutes once or twice a day will be unlikely to cause this lesion and may even prevent it. Toxicity to the CNS is very unlikely to occur at 2.0 atm abs or less, as it usually occurs in compromised patients treated at much higher pressures (3.0 atm abs). Pulmonary oxygen toxicity in general, is not seen in HBO2 protocols. It is sometimes seen in the treatment of divers when long periods are spent at high pressure -typically 2.8 atm abs on military therapeutic tables. Probably this type of oxygen toxicity is related to the action of reactive species of oxygen (free radicals) on the lipid part of surfactant (DPPC). Nevertheless, in our experience we have only found pulmonary oxygen toxicity in neonates with history of hyaline membrane and/or bronchopulmonary dysplasia after 1 or 2 treatments. In uncompromised neonates it takes more than 2 treatments to see evidence of toxicity. Fortunately, it responds well to inhaled steroids and/or surfactants. Special Considerations in the Management of Neonates There are several factors which should be considered in the management of neonates under hyperbaric conditions, especially in a monoplace chamber. 1. Our studies have involved patients older than 34 weeks of pregnancy and above 1.2 kg. 2. The patient should always be accompanied by a neonatologist and/or hyperbaric physician, as an inside attendant. 3. There is no ventilator suitable for these patients and they should be bagged when necessary by the inside attendant. 4. To avoid hypothermia, all the clothes (100% cotton) used to cover the neonates should be warmed in a vapor autoclave and kept at 38C before covering the patient (never heat them in a microwave oven because of the risk of ignition). 5. A transcutaneous oxygen monitor (TCOM) can be used in the second left intercostal space, or around that area, as an indirect measure for adequate ventilation and oxygenation. A reading should be taken at normal atmospheric pressure when the patient has a haemoglobin saturation of 95% and this can be used as a baseline. If during HBO2 the patient has a value below the baseline, there is a problem with the ventilation of the patient. 6. Our treatment protocol for neonates is 2.0 atm abs for 45 minutes (20 min oxygen, 5 min air, and 20 min oxygen) qid or bid. 7. In neonates the CNS oxygen toxicity is rare, but pulmonary oxygen toxicity is not. Special care should be taken for patients with history of hyaline membrane and/or bronchopulmonary dysplasia. It can be handled with preventive inhaled steroid and/or surfactant. Those patients that develop pulmonary oxygen toxicity

should receive inhaled steroids and/or surfactant before the next treatment 8. Evaluation of the eye in neonates is important. It should include fundascopic examination and/or visual evoked potentials. Always get a baseline and we have continued follow up every month until 18 months of age. Conclusions: Neonates require special handling in a hyperbaric chamber, particularly in a monoplace unit. It is mandatory to have an inside assistant and to do other measures (mentioned above) to provide an adequate inside environment for the neonate. They are also specially prone to oxygen toxicity, particularly of the lungs. Nevertheless, they respond very quickly and may require only one treatment to resolve the local ischemic/hypoxic condition and the systemic response (DIC, SIR, or shock) to this event. We observe that these patients treated early (<6 h of the event) have dramatic reversal of their condition and HBO2 is a safe and cost-effective adjunctive treatment. There is a need to undertake large randomized, controlled studies to establish the efficacy of HBO2 in ischemic/hypoxic conditions. REFERENCES: 1. Hyperbaric Oxygen Therapy: A Committee Report. Undersea and Hyperbaric Medical Society, Inc. Bethesda, Maryland, 1992. 2. Martorano F.J, Hoover D. The child hyperbaric patient. J Hyper Med 1988;1:15--21. 3. Monies-Chass I, Herer D, Alon U, Birkhann J. Hyperbaric oxygen in acute ischaemia due to allergic vasculitis. Anaesthesia 1976;31:1221-1224. 4. Boerema I, Meije NG, et al. Observations during operations on deeply cyanotic young children breathing oxygen at three atmospheres absolute. Ped Surg 1962; 52:796-799. 5. Thombs PA, Martorano FJ. Hyperbaric Medicine in Pediatric Practice. Hvperbaric Medicine Practice 1994:262-275. 6. Santamaria JP, Williams ET, Desautels DA. Hyperbaric oxygen therapy in pediatrics. Adv Pediatr 1995;42:335-386. 7. Rosenthal E, Benderly A, Monies-Chess I, et al. Hyperbaric oxygenation in peripheral ischemic lesions in infants. Arch Dis Childhood 1985;60:372-374. 8. Sanchez EC, Myers RAM. Hyperbaric oxygen therapy in the pediatric patient of 20 year experience. Undersea Biomed Res 1992;19(Suppl):109. 9. Kuzemko JA, Loder RE. Purpura fulminans treated with hyperbaric oxygenation. South Western Med J 1990;4:157. 10. Waisman O, Shupak A, Weisz H, Melamed Y. Hyperbaric oxygen therapy in the pediatric patient: the experience of the Israel Naval Medical Institute. Pediatrics 1998; 102: 53-89. 11. Bayboradov BD. Some specifics in the application of hyperbaric oxygenation in the treatment of acute respiratory insufficiency in newborn Infants. Proceedings of the7th International Congress on Hyperbaric Medicine, Moscow, 1981:299-312. 12. Kostyvkov W, Borisenkov YV, Gerosimovakays OI. Anesthesiologlcal support of surgery under conditions of hyperbaric oxygenation of young children with congenital heart defects. Proceedings of the 7th International Congress on Hyperbaric Medicine, Moscow, 1981:623-628. 13. Pilinoga VG, Konciratenko VI, Timoshenko NA. Application of hyperbaric oxygenation in newborns with intracranial birth trauma, Proceedings of the 7'" International Congress on Hyperbaric Medicine, Moscow, 1981:202:294. 14. Soravik P1. Hyperbaric oxygenation in complex therapy of acute hematogenic osteomyelitis in children. Proceedings of the 7'" International Congress on Hyperbaric Medicine. Moscow. 1981:565-574. 15. Sorovik P1. Complex treatment of acute hematogenic osteomyelitis of newborns and infants with the use of dioxide and HBO therapy. Vesn Khir 1980;124:135-138. 16. Estrin W, Volt VE, Gasova LA, S al. The effect of hyperbaric oxygenation on the mechanisms of adaptation to hyperoxia in septic aggression in infants. Proceedings of the 7th International Congress on Hyperbaric Medicine, Moscow, 1981:343. 17. Anokhin Ml, Baydin SA, Kazanski OD, et al. Cardiorespiratory control of the effectiveness of the sessions of hyperbaric oxygenation in children. Proceedings of the 7th International Congress on Hyperbaric Medicine, Moscow, 1981: 18. Barrie H. Hyperbaric oxygenation

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There certainly have been a number of reports regarding significant benefits for diabetic patients suffering from diabetic side effects such as non-healing foot ulcers and retinopathy. My own personal experience adds to this. I have treated myself with HBO2 for 18 months for multiple dystonias, with great success. I wrote a detailed report to this list entitled "Hyperbaric Oxygen Treatment of Chronic Dystonias" on 18th March this year. Because it was my very clear intention to focus interest on the use of HBO2 for treating dystonias and, possibly, other neurological movement disorders such as dyskinesias, I did not include in that post the other benefits that I had gained from my treatment. I have suffered from diagnosed diabetes for some nine years, keeping blood glucose under quite good control with tight dietary control, plenty of exercise and a modest rate of medication with tolbutamide. From the time of diagnosis I already suffered from neuropathy on most of the left side of my left foot, with essentially no sensations of feeling in that area. While the neuropathy did not deteriorate much over the years, probably because of the good control of blood glucose, from about four years ago, until I started HBO2 in January 1998, I started

displaying small microaneurysms in the retinas of my eyes and I also seemed to be moving steadily towards developing glaucoma - the internal pressures in both my eyes had risen from the normal sub-20 mm Hg to 32 and 34 mm Hg respectively in my two eyes by late 1997. The only reason I had not started direct treatment of the incipient glaucoma was because there was at that time no damage yet showing to the optic nerve and no reduction in field of vision. However, I was having frequent check-ups with an eye specialist regarding both the microaneurysms (which could progress to retinopathy in the eyes and to all sorts of other nasties elsewhere in the body) and the potential glaucoma. After my first 20 treatments with HBO2, the neuropathy in my left foot had completely gone (and has remained clear ever since), the microaneurysms had completely gone with no recurrence since and my internal eye pressures are back under 20 mm Hg in both eyes and have been stable that way for nearly 18 months now. Do remember that it is the complications that develop from diabetes that maim and kill, rather than the diabetes itself. Having now added the information regarding the dramatic improvement in my diabetic complications, I might as well also share with you the fact that regular HBO2 has also controlled what had been fairly severe cervical osteoarthritis into a problem of a degree of restricted neck movement. Prior to the HBO2 treatment regime, I had inflammation 'flare-ups' of the arthritic areas that would happen once or twice a month and last with severe pain for several days each time. I have had NO severe inflammation in the 18 months of regular HBO therapy. This fully supports the information often posted by Dr. Philip James that oxygen is a powerful anti-inflammatory agent for the body. You will realise that HBO has actually transformed my life even more than indicated by my post regarding dystonias. I did not include the other results because I feared readers would think that I was exaggerating and it might have prevented the stimulus that I was trying to give for dystonia treatment with HBO2. For the 'doubting' neurologists, I would argue that my benefits in relation to two different neurological conditions, namely chronic multiple dystonias and diabetic neuropathy, strongly support all the other evidence of the potential power of HBO2 therapy in neurological conditions, as so ably argued and often proven by such experts in the field as Drs. Philip James and Richard Neubauer. Best regards to all HBO supporters - John Armstrong.

Hyperbaric medicine is really not in its infancy - the first publication on the use of oxygen under hyperbaric conditions is in the Lancet for 1887. The difficulty is that the standards required for pharmaceuticals are being applied to the use of oxygen and even when a superb double-blind trial is undertaken it is ignored as in the case of Fischer et al's publication in the NEJM on multiple sclerosis. Until EVERY physician - not hyperbaric physicians - feels comfortable prescribing a course of oxygen therapy, oxygen will never be properly used. The real issue in hyperbaric oxygen therapy is the use of a chamber to deliver oxygen and it is very clear that most physicians are terrified by chambers and the technology although most would never admit it. Best wishes, Philip James

I've always been of the opinion that the reason HBO2 is so widely ignored by physicians in the U.S., regardless of scientific studies--is ultimately attributable to Medicare. Though Medicare has a restricted list of indications that it will pay for, the list is only the beginning. Medicare has a 100% audit rate (in Georgia and perhaps elseware) and then pays poorly and slowly or not at all. Other insurers take their cues from Medicare. The fact is that any physician in private practice who treats patients with HBO2 must spend a disproportionate

amount of time dealing with insurers or go out of business. No politically connected group is screaming for HBO2 so academic physicians can't find government grants for HBO2 research, and unlike the deep pocket ethical pharmiceutical companies, the small companies who make HBO2 equipment haven't the funds to pay for research. That leaves a small band of private practitioners and an even smaller band of academicians who continue to play the game despite the stacked deck. Unfortunately, Medicare shows no signs of changing and even the politicians are afraid to get near it. Sorry if I sound negative, but thems the facts. Glenn L. Goodhart, M.D., J.D., www.atlantahyperbaric.com

The fundamental technology in a hyperbaric chamber system is fairly simple and well understood. However, the proper packaging of that technology into a safe and effective medical instrument is a lot more difficult than it looks. The following points must be considered: 1. A clinical chamber system is NOT a diving recompression chamber that happened to come indoors. The main personnel hazard in a clinical chamber, for example, is often not the much discussed issues of oxygen toxicity or fire, but back injuries to staff from handling patients. 2. Hyperbaric chambers ARE pressure vessels. As such, in most jurisdictions (state, province, etc.), they are subject to the boiler and pressure vessel laws of that jurisdiction. This regulatory aspect has nothing to do with medicine, just basic public safety issues related to pressure vessels. 3. Clinical hyperbaric chambers ARE medical devices. In the United States they are subject to the FDA's rules for Class II medical devices. As such, a clinical hyperbaric chamber manufacturer is required to have a "pre-market market clearance" from the FDA before the device can be legally marketed or placed into commercial distribution. This clearance is often called a "510(k) clearance" because of the number of the form on which the clearance request must be submitted. In Canada, clinical hyperbaric chambers are subject to the rules for Class III medical devices under rules managed by the Bureau of Medical Devices of Health Canada. The Canadian rules for Class III devices are similar to the US FDA rules for Class II devices. However, the current Canadian rules are "young" in a regulatory sense having gone into effect in July 1998. Consequently, awareness of even the existence of the rules is far from universal and understanding of their requirements is even less universal. An article titled "Regulatory Issues: The Role of the FDA" was published in the spring 1997 issue of "Triage", the journal of the National Board of Diving and Hyperbaric Medical Technology (NBDHMT). A data base of all medical devices, including hyperbaric chambers, with pre-market clearances is maintained on the FDA website. Medical devices produced in an unregistered establishment and/or sold without a pre-market clearance are considered by the FDA to be "adultered", and therefore prohibited. FDA rules also prohibit manufacturers from including the fact that they have an FDA clearance in their advertising. Consequently, the only ways for a prospective purchaser to determine the existence of a necessary pre-market clearance are to either ask the manufacturer or ask the FDA, and the most time efficient way (by far) to ask the FDA is to access the FDA's website. To legally sell chambers in Canada, a clinical hyperbaric chamber manufacturer is required to be registered as a manufacturing establishment with Health Canada (equivalent to a Ministry of Health) and have a Canadian medical device license covering each model offered for sale. One can access general rules for medical devices in Canada on-line. However, the Canadian medical device license data base itself is accessible only internally by Health Canada professionals. Further, given the relative "newness" o

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