

HBOT...What Hyperbaric Oxygen Therapy Can Do For Your Patients 2014

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Introduction

Hyperbaric oxygen therapy [HBOT] has transcended from its traditional place in treatment of decompression illness ["the bends"] to a variety of clinical applications globally. Basic science studies have demonstrated HBOT effects and mechanisms of action. Evidence based reviews and meta-analyses have been published on HBOT's beneficial effect on humans with extreme anemia and in wound healing [22, 24]. Clinical studies on practical applications are abundant in the human medical literature. Book chapters describing clinical applications of HBOT have been included in the most recent editions of Ettinger's "Textbook of Veterinary Internal Medicine" and Bonagura's "Current Veterinary Therapy XV". The June 2010 Veterinary Emergency and Critical Care Journal featured HBOT as the subject in its 'State of the Art' articles [17]. Recently, Dr. Colin Kaide [from The Ohio State University Medical Center] discussed HBOT and its role in the therapy of human infectious diseases in The Emergency Medicine Clinics of North America [18]. He concluded with the statement "in our opinion withholding HBOT because of a lack of randomized trials in the face of a huge body of clinical experience and in vitro studies, especially in these devastating disease processes, would be bordering on unethical". The Veterinary Hyperbaric Medicine Society [VHMS] has developed didactic material and test questions for hyperbaric oxygen therapy technical certification. HBOT research has reached the point that studies are demonstrating the specific treatment pressures which are most effective at altering inflammatory gene expression (32). This presentation will focus on HBOT treatment methods, physiologic effects, therapeutic effects, clinical uses, and safety issues in veterinary medical cases. We will describe evidenced based studies. Specific citations of the literature and examples of patients treated with HBOT will be presented.

HBOT Chambers and Ancillary Hardware

Modestly priced therapeutic chambers are now available from medical equipment suppliers. Small animal sized veterinary models have been manufactured. Experienced professionals are available to assist in designing systems, obtaining and installing chambers, training hospital personnel regarding operation and safety issues, and servicing HBOT equipment. Clinical chambers range in size from monoplace [single patient] design, to chambers accommodating multiple patients / caregivers, and operating suites. Most chambers require an oxygen supply system capable of large gas volumes delivered at a rapid flow rate. Liquid oxygen tanks and a medical grade oxygen pipeline of large diameter satisfy these requirements. A passive discharge pipeline directs the exhaust gases outside the hospital building. Some chambers have ports allowing [specific] IV lines and/ or tubing for assisted ventilation to be connected to the patient during an HBOT session. Current oxygen costs to operate a small animal monoplace chamber may range from approximately \$4 to \$20 per treatment session depending on chamber design, length of session, pressure employed, and oxygen supply system. The clinician should recognize that a distinct difference exists between Hyperbaric Oxygen Therapy and "Minimal" Hyperbaric Oxygen Therapy. The portable, [usually vinyl, plastic, and fabric] balloon type chambers marketed for "Minimal" HBOT do not operate at pressures or oxygen concentrations in the typical therapeutic ranges of the medical grade hyperbaric oxygen chambers.

Treatment Protocol ["The Dive"]

The patient is prepared by examination and body temperature determination. HBOT is generally not given when the small animal's patient's body temperature is greater than 103.5 degrees Fahrenheit. Theoretically, excessive hyperthermia may increase oxygen uptake by tissues, and enhance the chance of oxygen toxicity. The vast majority of patients are quiet and relaxed during HBOT. Occasional patients are given sedation. Acepromazine is the usual drug of choice for small animals. Occasionally, benzodiazepines or barbiturates are employed in canines. Cotton bandages cover IV catheters. Metal collars are removed. A static inhibitor ground plate is placed under the patient. The session begins with a gradual pressure increase to the designated treatment pressure over approximately 10-15 minutes. The desired treatment pressure may range from 1.5 to 3 atmospheres absolute [ATA] in a 100% oxygen environment. The treatment period "at pressure" may range from 45 minutes to 2 hours. Then, a gradual decompression over approximately 10-15 minutes is made, and the patient is removed from the chamber. Currently, most of our small animal patients are treated at 1.5 ATA for 45 minutes "at pressure". Patients with Lyme disease are treated with progressively increasing pressures, and then followed up with treatments at 2.4 ATA, which is bacteriocidal to the spirochete. In patients perceived to be at reduced threshold for seizures, one should employ a pressure of 1.5 ATA for the "at pressure" treatment period. The patients are rested at room atmospheric pressure for at least 4 hours between HBOT sessions to minimize the chances of CNS or pulmonary oxygen toxicity. We treat most patients with BID sessions, and continue HBOT acutely until marked and progressive improvement occurs [for example, the tetraparetic, paraparetic, or monoparetic patient is using the affected limb[s] with improving strength and function over several days, or the wound is well on its way to resolution]. We treat selected patients with follow up sessions after initial discharge from the hospital. In many cases dogs or cats may be treated as outpatients. Patients may receive as little as 1 session [for example, after orthopedic surgery or venomous insect bite when administered to reduce inflammation and swelling] to as many as 40 or more

sessions in extremely critical or chronic disease entities. One canine patient with multifocal CNS inflammatory disease received over 700 treatment sessions in 5 ½ years as her sole method of therapy for this clinical issue.

Physiology of HBOT

At normal atmospheric pressures [1 ATA] and while breathing room air, insignificant amounts of oxygen are dissolved and delivered to the tissues via the plasma. Mild increases are possible when oxygen is administered via mask, oxygen cage, intranasally, or intubation. The effects of HBOT are based upon the fact that oxygen delivered to the alveoli under increased atmospheric pressure results in large increases in the amount dissolved in plasma. This can increase the plasma arterial oxygen content from 0.32 vol % [ml O₂/ dl whole blood] breathing room air at 1 ATA, to 4.44 vol % at 2 ATA breathing 100% oxygen, and up to 6.8 vol % at 3 ATA breathing 100% oxygen. This dramatic increase in dissolved oxygen [for example, breathing 100% oxygen at 3 ATA] allows diffusion and delivery via the plasma up to 4 times further through the tissues than is possible while breathing room air at 1 ATA. This delivery is independent of the hemoglobin system. Tissue PO₂ measurement devices have demonstrated that oxygen tension remains elevated at > 10% of normal for up to 3 hours following a 1 hour HBOT session.¹ Thus, cells and mitochondria in areas where nearby capillary blood flow has been compromised by traumatic, ischemic, or inflammatory processes may receive oxygen subsequent to HBOT which would otherwise be denied by the underlying pathological disease process. Hyperbaric oxygen at 2 ATA has been shown to reduce cerebral blood flow up to 25% [by effecting vasoconstriction], yet concurrently increase [X 10] cerebral oxygen content. Intracranial pressure and cerebral edema are reduced following HBOT. In addition to the direct action of supplying oxygen necessary for mitochondrial metabolic processes, HBOT creates short pulses of increased reactive oxygen species [ROS] and reactive nitrogen species [RNS]. These molecules act in conjunction with redox systems involving glutathione, thioredoxin, and pyridine nucleotides to coordinate cell signaling and anti-oxidant, protective pathways [23]. Some of the results of these reactions are listed below:

- An increase in neovascularization [new blood vessel growth]. HBOT induces the production of vascular endothelial growth factor [VEGF]. (3, 19, 20)
- Enhancement of white blood cell oxidative killing and antibacterial effects [29]
- Potentiation of the cidal or static antibacterial effects of antibiotics such as the fluoroquinolones, aminoglycosides, vancomycin, and sulfas [29]
- Stimulation of nitric oxide synthetase [20]
- Modification of cytokine effects by regulating production and affecting receptor sites [anti-inflammatory]. HBOT Modulates MMP balance [anti-inflammatory][5]
- Inhibition of neutrophil adherence to microvascular endothelia, resulting in SUPPRESSION of the deleterious cascade of events that follows in ischemia- reperfusion injury. HBOT has been found to inhibit free radical formation. (4)
- Multiplication and mobilization of vasculogenic stem/progenitor cells [SPC's] which can be demonstrated in blood, tissue and in certain matrix materials implanted throughout the body[23].
- An increase of a key subset of SPC's, endothelial progenitor cells [EPC's]. EPC's have the ability to "home" to the site of tissue injury or dysfunction, differentiate into mature cells, and participate in vascular repair. This augmentation of SPC recruitment and differentiation is ascribed to HBOT's engagement of a physiological autocrine activation loop involving a complex set of responses initiated by the intracellular proteins thioredoxine, hypoxia inducible factor – 1, and hypoxia inducible factor – 1 – dependent growth factors. (19, 20)
- Modification of cellular responses at the level of genes [23,32]
- Increased ERK 1/2 levels and up-regulation of PDGFR-R expression leading to accelerated wound healing[25]
- Down regulation of ICAM-1 expression
- Reduction in the size of intravascular gas bubbles [air emboli] by the direct effect of Boyle's Law

Three recent textbooks and other publications offer detailed discussions of the physiology of oxygenation, its relation to HBOT, and effects on the CNS, PNS, and pathological disease states including the wound healing process [2,3,4,19, 20, 29].

Therapeutic Effects and Clinical Uses

The most common case types treated with HBOT at our small animal facility include intervertebral disc disease, pre and post op spinal and orthopedic surgical cases, acute severe anemia, ischemic syndromes, post cardiopulmonary arrest, immune mediated diseases, fibrocartilagenous emboli, pancreatitis, head trauma, snake bite, sepsis, and wound care. We describe case types and examples with associated literature references in the remainder of this discussion.

Exceptional Anemia Secondary to Blood Loss or Hemolytic Etiologies

HBOT should be considered in patients with severe anemia while cross-matching before transfusion, and after the transfusion of stored blood cell preparations. HBOT can provide necessary oxygen to ischemic systemic tissues through plasma delivery of oxygen. HBOT effectively reduces the critical "Oxygen Debt" which develops in severe anemia prior to presentation and treatment. Studies have shown that in hemolytic anemia endogenous carbon monoxide [CO] is produced as heme is catabolized. This blocks oxygen binding sites on viable remaining RBC's. CO also binds to myoglobin and to mitochondrial cytochrome, and reduces vital red blood cell deformability. Poorly deformable RBC's cannot pass freely into and through the deep tissue microcirculation. CO causes a shift of the oxygen dissociation curve to the left. HBOT markedly shortens CO half-life, and reverses these adverse physiological processes. Stored blood

products used for transfusion have poor RBC deformability, and their oxygen dissociation curve is shifted to the left as well. These transfused “stored” RBC’s can carry oxygen, making the mucous membranes appear “pink”, but cannot

effectively release the oxygen to the tissues until the curve shifts to the right. It can be many hours after transfusion before the viable RBC’s in stored blood become deformable and shift their oxygen dissociation curve toward the right. HBOT can hasten these processes while it supplies oxygen to the systemic tissues in need. [21] Hyperbaric oxygen therapy has saved the lives of many severely anemic Jehovah’s Witnesses, who do not allow transfusion in the practice of their religion. There is an extensive evidence-based review demonstrating the benefit of HBOT in the treatment of severe anemia in human medicine. [22] HBOT can be employed in situations where compatible blood is difficult to obtain or not available, as in felines with “Type B” blood.

Sepsis

Humans and mice with sepsis exhibit reduced red blood cell deformability as a part of the pathophysiology of this disease process [30]. A course of HBOT can supply the deep tissue beds with oxygen, which cannot be delivered into the microcirculation by the non-malleable RBC’s. Adjuvant HBOT also potentiates certain antibiotic classes [for example, quinolones and aminoglycosides], and inhibits neutrophil adherence to endothelial membranes.

Snakebite

Snakebite pit viper envenomation is the classic example of the clinical situation where the anti-inflammatory, tissue sparing and tissue healing effects of HBOT come together to create dramatic changes in many patients. If a canine snakebite patient is rapidly placed into an HBOT chamber within a few hours of the bite event, grossly visible swelling is often markedly reduced during and after the treatment session [with or without anti-venin administration]. HBOT may also be effective in many snakebite cases in the face of delayed treatment.

Complete Global Cerebral Ischemia

A 1992 paper² described a controlled study from Japan where 20 dogs with complete global cerebral ischemia of 15 minutes duration were randomized and divided into two groups. One group received 1 hour sessions of HBOT at 3 ATA in 100% oxygen at 3, 24, and 29 hours after recirculation was established. The control group received room air at 1 ATA. Both groups received nursing support. The HBOT treated group’s mean neurologic recovery score was > 65/100 after 5 days, with neurologic recovery scores of > 95/100 reached in two dogs from the HBOT group [range: 0=brain dead to 100= normal]. In contrast, in the group not receiving HBOT, the mean neurologic score remained < 60/100 throughout the 14 day follow up, and only 1 of 10 dogs from the non HBOT group recovered to a score of > 65/100. 7 of the HBOT group survived to the 14 day follow up, whereas 3 of the non HBOT group survived to the end of the 14 day follow up.

Case example: A 1 year old M/I Shih-Tzu canine fell off a grooming table while the groomer was distracted, and was accidentally hung by the lead around the neck. CPR was successful. Acute cortical blindness followed. The patient was given IV methylprednisolone immediately following the resuscitation, and referred for hyperbaric therapy the following day. Low dose oral prednisolone was continued. BID HBOT [45 minute sessions at 2 ATA] was given for 7 days. After the second session vision began to return as evidenced by obstacle course performance. Two week follow up confirmed improving vision based on owner interview and obstacle course examination. Consultation by an ophthalmologist confirmed resolving cortical blindness. In human cases [near hanging, near drowning, neonatal asphyxia, stroke, cardiopulmonary arrest, etc.] SPECT brain blood flow imaging has been used to demonstrate abnormalities in cerebral perfusion and subsequent improvement following immediate and long term HBOT. HBOT is often employed in cases of birth asphyxia in foals.

Referral for HBOT therapy after cardiopulmonary arrest during anesthesia or after injury has become more frequent as primary care veterinarians recognize the option exists.

Head Trauma

Many studies have shown that HBOT reduces elevations in intracranial pressure resulting from head trauma in animals and in human head trauma patients.⁴ Clinical trials have demonstrated improved survival rates and neurologic recovery scores in human head trauma patients³. In addition, improved glucose utilization in rat brain tissue has been demonstrated to persist for up to 24 hours following the last HBOT.⁴ There is much contemporary focus and research on the role of matrix metalloproteinases [MMPs] in traumatic brain injury and inflammatory CNS and PNS diseases, including Multiple Sclerosis [MS] in humans. A change in the balance of certain types of these proteases is associated with cellular infiltrates, apoptosis, and gliosis in traumatic, inflammatory, and neoplastic CNS disease. A 2006 rat model study of traumatic brain injury demonstrated that subjects treated with HBOT had reduced expression of certain MMPs, milder neutrophilic inflammatory infiltrates, and decreased secondary cell death when compared to controls.⁵

Case example: 3 month old F/I canine Yorkshire Terrier hit by a recliner chair. The patient presented obtunded and able to posture only when placed sternally. IV mannitol and ICU oxygen unit therapy were given, and a neck brace placed overnight by the E/CC clinicians. BID HBOT was begun the following morning [45 minute sessions at 2 ATA] and continued for 5

days. Marked neurologic improvement was obvious as the patient exited the chamber after the first session, and progressed rapidly until discharge.

Fibrocartilagenous Emboli

Some HBOT studies performed on dogs date back several decades. A 1965 study demonstrated that spinal cord pO₂ could be raised by HBOT as long as 72 hours after tissue hypoxia was created in a model of spinal cord injury in canines.⁶ Canine cases of fibrocartilagenous emboli often show rapid improvement when promptly treated by HBOT. It is especially important for nursing care and physical therapy purposes to get these primarily large breed patients ambulatory as soon as possible.

Case examples: 1] 8 year old M/N Labrador mix . Acutely monoparetic, then paraparetic. 2] 8 year old F/S Boxer. Acutely monoparetic. Clinical diagnoses were based on neurologic examinations, CSF analysis, and myelograms within a few hours of emergency presentation. Both patients received one dose of parenteral corticosteroids, then low dose short term oral prednisolone. Both patients were given BID HBOT [45 minute sessions at 2 ATA] . The Lab received 14 HBOT treatments, the Boxer 10. It is interesting to note in this acute ischemic myelopathy that patients will often improve markedly as they exit the chamber session, then regress, presumably as pO₂ in the affected cord region drops off. Patients who exhibit this pattern typically improve for longer periods after each session, and eventually maintain their neurologic improvement.

Spinal Cord Trauma, Intervertebral Disc Disease, and other Compressive Spinal Cord Lesions

In a 1972 canine model of spinal cord compression, spinal cord tissue pO₂ in the normal cord rose when the subjects were breathing 100% oxygen at 1 ATA (Normobaric Oxygen). After compressive trauma, the cord pO₂ dropped to near zero on room air, and did not rise when the subjects were breathing 100% oxygen at 1 ATA. When HBOT at 2 ATA was given with 100% oxygen, tissue pO₂ rose sharply even during the compressive period. Neurologic recovery of the HBOT treated group was improved compared to the control group.⁷

Case example: 11 year old Bichon M/N. Acute upper motor neuron tetraparesis with severe neck pain. Normal CSF protein and cytology. Spinal stenosis at a C2-3 fusion site [no history of previous surgery or trauma] and a C3-4 disc extrusion were found on myelographic examination. Initial treatment was with HBOT [2 ATA, 45 minutes], prior to the diagnostics. At this point the patient became strongly ambulatory. Diagnostics were performed, followed immediately by a limited continuous dorsal laminectomy. Low dose oral prednisolone and HBOT were given post operatively for 6 days. Progressive clinical improvement was rapid. A desirable effect in neurosurgical cases treated with post op HBOT is rapid surgical wound healing, with reduced swelling, inflammation, seroma, and scar formation. HBOT has become standard pre and post neurosurgical adjunctive therapy in our practice, for both spinal and brain surgical cases. We have used HBOT in conservative treatment of documented or presumed spinal cord compressive diseases.

Inflammatory CNS Diseases

We have discussed some of the mechanisms of HBOT anti-inflammatory effects above. The reader should note that in the UK, there are 64 centers [distributed to cover the population density] which are dedicated solely to the treatment of MS in human patients. Over 1.7 million sessions have been completed in the last 24 years without serious incident.⁸ Patients generally manage their own long term treatment schedule, and many find that their symptoms, especially frequency of micturition, are controlled only by regular HBOT sessions. Some schedule their holidays to be near a "Center". The reader is referred to a detailed chapter on rationale for HBOT in inflammatory disease, including MS in a recent HBOT textbook.² A 2006 symposium presentation from a Russian HBOT research clinician described the use of combined HBOT and cyclosporine in the treatment of inflammatory CNS disease in humans⁹

Case example: 9 ½ year old M/N mixed canine presented for persistent fever, sudden loss of coordination and slight personality change. Neurologic exam supported multifocal CNS lesions. CSF cisternal and lumbar puncture protein and cytology were normal. MRI revealed multiple small mixed size hyperintense T2-weighted lesions throughout the thalamus and rostral brainstem. Most remained hyperintense on T2-weighted FLAIR sequencing. Multiple serologies and PCR's, PARR [LSA] were submitted. A 1/164 positive serology for E equi was the only notable laboratory finding. BID treatments of HBOT [45 minute sessions at 2 ATA over 7 days] were initiated along with cyclosporine, prednisolone, imidocarb, and doxycycline. Neurologic signs improved over a 7 day period, with the owner commenting on a marked improvement at home at the two week recheck exam. The immunosuppressive therapy was tapered very slowly over several weeks.

Major Organ Ischemia

HBOT may be employed in cases with major organ ischemia, such as post-surgical correction GDV in the canine, where the ischemia- reperfusion injury complex often results in serious clinical complications.

Pancreatitis

This inflammatory process is often severe, effusive, and fatal to canine and feline patients. Recent publications describing experimental rat pancreatitis models demonstrate reduced histopathologic severity and improved survival rate in the groups exposed to HBOT when compared to controls.^{14,15,16} Current pathophysiology extrapolated from experimental models and human medicine incriminates ischemia, along with neutrophil migration and adhesion to the endothelial walls following the initial activation of pancreatic enzymes locally. During the disease process upregulation of intercellular adhesion molecule -1 [ICAM-1] occurs, promoting neutrophil adhesion and the subsequent inflammatory cascade [26]. In addition to increasing oxygen to the swollen and inflamed pancreas, HBOT has been demonstrated to downregulate ICAM-1 expression [27], thus

reducing the tendency for neutrophils to adhere to the vascular endothelium. Our clinical experience is that now even cases with severe, effusive pancreatitis can be given a prognosis which includes a good chance for survival when HBOT is employed along with intensive supportive care. Case example... 12 year old Fe spayed Lab who ate a "rotted carcass" in a nearby yard. History, clinical signs, physical exam, radiographs, ultrasound exam, fluid analysis, and PLI all supported a diagnosis of pancreatitis. Severe pleural effusion was also present. BID HBOT for 45 minutes at 2 ATA was given. Traditional supportive care was continued. By hospitalization day 3 the pleural and peritoneal effusions were nearly resolved. A total of nine sessions were given, and rapid clinical improvement resulted in discharge by day 5. Physical exam one week after discharge was normal. Follow up PLI and ultrasound exam of the chest and abdomen 3 months later were normal.

Smoke Inhalation/ CO Toxicity/ Burn Wounds from Exposure to a Fire

This combination of pathology is a unique opportunity to treat three different clinical issues with one form of adjuvant therapy, HBOT.

Osteomyelitis/ Infectious Agents

The anti-inflammatory and angiogenic effects of HBOT are ideal here. HBOT potentiates the effect of certain antibiotics [for example, the quinolones and aminoglycosides], and is directly bacteriocidal to anaerobic bacteria. At 2.4 ATA HBOT is bacteriocidal to *Borrelia burgdorferi* [the Lyme disease spirochete][31]. Patients with Lyme disease are managed by gradually and progressively increasing treatment pressure from 1.5 ATA to 2.4 ATA, and continued with a course of 2.4 ATA sessions. This helps to reduce the severity of the Jarish-Herxheimer reaction as the organisms are destroyed.

Delayed or Non-Healing Wounds, Accelerated Healing of Exceptional or Large wounds, Crushing wounds

HBOT is widely accepted in human medicine for its adjuvant effect in wound healing, especially in diabetes mellitus or vascular occlusive disorders. It is a coded and reimbursed treatment modality for radiation induced tissue damage and non-healing wounds. As previously discussed, meta-analyses have demonstrated the benefit of HBOT in wound healing [24]. In addition to its enhancement of local wound tissue oxygen tension and vasculogenic effects, HBOT directly modulates intracellular signal pathways [comparable to peptide growth factors], and up-regulates PDGF-R expression, activating fibroblasts using a similar transduction cascade as traditional peptide growth factors, resulting in accelerated wound healing [25].

Osteoarthritis

The effects of HBOT on multiplication of circulating stem cell numbers and up-regulation of PDGF-R expression can be used to the patients' advantage when employing "Platelet Enhancement Therapy" in the management of osteoarthritis[20,25].

Other clinical applications of HBOT

Other cases treated with HBOT therapy include acute tetraparesis secondary to Atlanto-axial [A/A] luxation, acute peripheral nerve injury, and brain lesions pre and post operatively. Decubital ulcers, thermal burns, shearing wounds, and near drowning are a few of the other clinical applications for which we have employed HBOT. Human medical practice is often limited by "approved indication lists" and diagnosis "codes". For example, in the U.S., there are currently 14 indications approved by Medicare, and thus typically funded by third party payers. HBOT for Non-healing wounds of certain types is funded by some third party payers. The U.K. has 13 "approved" indications, Japan 20, China 53, and Russia 85. In the latter three countries the "approved" lists contain disease indications which translate as "severe spinal cord disorders", "acute and severe hypoxic brain disorders", "severe spinal cord injury", "Bell's palsy", "Multiple Sclerosis", "cranial traumas", "viral encephalitis", "illius", "sepsis", "non-healing wounds", "osteomyelitis", "burns", "mountain sickness", etc.

Bubbles

HBOT is the treatment of choice for arterial, venous, pulmonary, or cerebral air embolism. In veterinary medicine air embolism may occur as the result of complications resulting from central venous lines, interventional procedures, surgical procedures [such as C-section], and the ingestion of hydrogen peroxide or the use of hydrogen peroxide on well vascularized wounds.

Safety Issues

HBOT should not be administered to patients with pneumothorax, certain older type pacemakers, within 7-10 days after doxorubicin, or in a patient currently receiving cis-platinum or bleomycin. Acetazolamide, Zonisamide, or other carbonic anhydrase inhibitors should be tapered prior to HBOT, as they inhibit oxygen induced vasoconstriction and increase blood flow to the brain, increasing the chance of oxygen toxicity. Transdermal patches should be temporarily removed. Conservative dosages of narcotic analgesics should be employed prior to HBOT, as increased CO₂ tension secondary to respiratory depression can cause cerebral vasodilatation and predispose to oxygen induced seizures. Insulin dosages should be tapered prior to HBOT therapy. Patients with hyperthyroidism also may have an increased chance for oxygen induced seizures. Vestibular signs may be aggravated due to barostimulation of the ear structures. This said, at the AERC we have witnessed less than 40 short motor seizures in over twenty-seven thousand individual HBOT treatment sessions at our hospital over the past decade. The seizures all ended rapidly, and a gradual reduction in treatment pressure after the seizure activity finished was

initiated in these individuals. No sequellae were recognized as a result of those seizures. The previously cited textbooks are a good source of detailed information on potential contraindications and specific interactions of HBOT with other therapeutic measures [28,29].

The chamber contains 100 % oxygen under pressure. Measures should be taken to reduce the chance of fire. The chamber should be grounded. A static grounding plate should be used in small animals. Hair coats should be gently wiped with a wet cotton towel. Cotton towels and bandages generate less static than polyester fibers. No flammable materials or electronic devices should be placed in the chamber. Metal cages should not be used in the chamber. No metal collars, polyester collars, or air-filled collars should be used. Skin staples should not be used, or should be wrapped/ covered in 100% cotton bandaging or stockinette. Metal external fixators must be covered in the same manner. No alcohol, Vaseline, or flammable based dressings should be used. An emergency master oxygen shut off valve should be installed and known by all personnel. A water based fire extinguisher should be close and functional. A textbook on hyperbaric safety is recommended.¹⁰

HBOT in Equine Racing Athletes

Under the care and direction of veterinarians some horses receive post-race HBOT as a method to reduce the inflammatory sequellae of a supreme racing effort, or in the treatment of orthopedic or neurologic injuries.

In the spring of 1999 equine treatment chambers in trailers began appearing near racetracks in New York and California, as some trainers of equine athletes around the world began to use HBOT in their horses. No governing body was consulted initially, which resulted in New York racing officials issuing an immediate 7 day ban on HBOT for racing horses. After consultation with veterinarians familiar with HBOT, Maryland and New York have settled on a 48 hour pre- race moratorium on HBOT. Kentucky requires a 24 hour HBOT- free period prior to any race.

Conclusion

Over the past several years it has been very rewarding for the doctors and staff to observe the clinical improvement of many cases treated by HBOT at our hospital. The addition of this treatment modality has resulted in an obvious enhancement of our ability to successfully treat many critically ill patients.

¹ Wells, CH, et al. Tissue gas measurements during hyperbaric oxygen exposure, in Smith G [ed]. Proceedings of the Sixth International Congress on Hyperbaric Medicine. Aberdeen, Scotland, Aberdeen Press, 1977, pp 118-124

² Takahashi, M., et al, Hyperbaric oxygen therapy accelerates neurologic recovery after 15 – minute complete global cerebral ischemia in dogs. Critical Care Medicine, 1992;Vol.20,No.11:1588-1593

³ Holbach KH, et al. "Improved reversibility of traumatic mid-brain syndrome with application of hyperbaric oxygen pressure" Acta Neurochir. 1974;30:247-256

⁴ Contreras FI, et al. "The effect of hyperbaric oxygen on glucose utilization in freeze-traumatized rat brain" J Neurosurg. 1988;65:615-624

⁵ Vlodaysky, E et al. "Hyperbaric therapy reduces neuroinflammation and expression of matrix metalloproteinase-9 in the rat model of traumatic brain injury" Neuropathol Appl Neurobiol. 2006; Vol32, No. 1: 40-50

⁶ Maeda, N. "Experimental studies on the effect of decompression procedures and hyperbaric oxygenation for the treatment of spinal cord injury" J Natl Med Assoc. 1965 Vol 16: 429-447

⁷ Kelly, DL. Et al. "Effects of hyperbaric oxygenation and tissue oxygen studies in experimental paraplegia" Neurosurg. 1972; Vol 36: 425-429

⁸ Neubauer, RA, 1st International Symposium for the Use of Hyperbaric Oxygenation in the Neurosciences, 2006, pp 78-9

⁹ Kazantseva, NV. 1st International Symposium for the Use of Hyperbaric Oxygenation in the Neurosciences, 2006, pp32-3

¹⁰ Workman, W. Hyperbaric Facility Safety: A practical guide, Flagstaff, Az. Best publishing, 1999

14 Mas et al, "Hyperbaric oxygen induced changes in bacterial translocation and acinar ultrastructure in rat acute necrotizing pancreatitis" J Gastroenterol, 2005, Vol 40, No. 10, 980-98

15 Cuthbertson, CN et al, "Hyperbaric oxygen reduces severity and improves survival in acute pancreatitis ", abstract from the 36th annual meeting of the American pancreatic association, Nov 3-4, 2005

16 Chen et al, "Hyperbaric oxygen therapy attenuates pancreatic microcirculatory derangement and lung edema in acute experimental pancreatitis in rats", Pancreas, 1998 Jul; 17[1]: 44-9

17 Edwards, ML. "Hyperbaric oxygen Therapy, History, Principles, Applications in Disease", J Vet Emerg Crit Care, Volume 20, Nimer 3, June 2010, 289-298

18 Kaide CG. , "Hyperbaric Oxygen therapy: Applications in 'Infectious disease" , Emergency Medicine Clinics of North America, 26[2008], 571-595

19 Milovanova, TN, et al. "Hyperbaric oxygen stimulates vasculogenic stem cell growth and differentiation in vivo", J Appl Physiol 106: 711-728, 2009

20 Thom, SR, et al. "Vasculogenic stem cell mobilization and wound recruitment in diabetic patients: Increased cell number and intracellular regulatory protein content associated with hyperbaric oxygen therapy" Wond Rep Reg (2011) 19 149-161

21 Myking O. Schreinen A. Hyberbaric oxygen in hemolytic crisis. JAMA 1974;227:1161-1162

22 Van Meter KW. A systemic review of the literature reporting the application of hyperbaric oxygen in the treatment of exceptional blood loss anemia: an evidence based approach. Undersea hyperbaric medicine, Vol 32, No1, 2005, 61-79

23 Thom SR. "Hyperbaric Oxygen-Its Mechanisms and Efficacy, Plast Reconstuct Surg 2011 January, 127 [Suppl 1]: 131S-141S

-
- 24 Goldman RJ, "Hyperbaric Oxygen Therapy For Wound Healing and Limb Salvage: A Systemic Review", *Physical Medicine And Rehabilitation*. 2009;1:471-489
- 25 Saulis AS et al, Hyperbaric Oxygen Modulates PDGF Receptor Beta Expression and ERK 1/2 Activation in Human Dermal Fibroblasts In Vitro, *Proceedings, Undersea and Hyperbaric Medical Society*, 2000
- 26 Mansfield, C, "Pathophysiology of Acute Pancreatitis: Potential Application from Experimental Models and Human Medicine to Dogs", *J Vet Intern Med* 2012;26:875-887
- 27 Buras JA, et al, "Hyperbaric oxygen downregulates ICAM-1 expression induced by hypoxia and hypoglycemia: the role of NOS", *Am J Physiol Cell Physiol*. 2000 Feb;278[2]:C292-302
- 28 Jain KK, *Textbook of Hyperbaric medicine*, 5th revised edition, Hogrefe, 2009
- 29 Kindwall and Whelan, *Hyperbaric Medicine Practice*, second edition revised, Best, 2004
- 30 Baskurt OK et al, Red Blood Cell Deformability in Sepsis, *Am J Respir Crit Care Med* Vol 157. pp 421-427, 1998
- 31 Fife WP, Freeman DM, Treatment of Lyme Disease with Hyperbaric Oxygen Therapy, Abstract, UHMS proceedings 1998
- 32 Kendall, AC et al, "Different oxygen treatment pressures after inflammatory gene expression in human endothelial cells", *VHM* 2013, Vol 40, No. 2, Pates 115-123.

Key Words

Hyperbaric Oxygen Therapy, HBOT, Hyperbaric Oxygen Chamber, Head trauma, Ischemia, Wound Healing, Pancreatitis, ROS, Anemia

