



**LITERATURE SEARCH REPORT: HYPERBARIC OXYGEN THERAPY (HBOT)  
USES IN VETERINARY HEALTH WITH AN EMPHASIS ON TRAUMA-RELATED  
USE CASES**

**REPORT PREPARED FOR:**

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## ABBREVIATIONS

<b>ARF</b>	Acute Renal Failure
<b>ATP</b>	Adenosine Triphosphate
<b>BioMDg</b>	Biologics & Medical Device Consulting Group
<b>CCI</b>	Chronic Constriction Injury
<b>DCS</b>	Decompression Sickness
<b>GFR</b>	Glomerular Filtration Rate
<b>HBO</b>	Hyperbaric Oxygen
<b>HBOT</b>	Hyperbaric Oxygen Therapy
<b>IR</b>	Ischemia-Reperfusion
<b>NBO</b>	Normobaric Oxygen
<b>NO</b>	Nitric Oxide
<b>ROS</b>	Reactive Oxygen Species
<b>VEGF</b>	Vascular Endothelial Growth Factor
<b>TBI</b>	Traumatic Brain Injury

**1. RESEARCHERS/INSTITUTIONS INTERESTED IN VETERINARY USE OF HBOT**

The following table summarizes institutions and clinics based in the United States who demonstrate an interest in HBOT research for veterinary use.

Table 1. Institutions with a Demonstrated Interest in Veterinary Use of HBOT

Organization / Institution	Comments
Veterinary Hyperbaric Medicine Society: Department of Small Animal Clinical Sciences, University of Tennessee	This group is quite prominent in veterinary applications of hyperbaric oxygen therapy. There are several researchers in the organization.  <a href="https://hyperbaricmedicine.com/courses/hyperbaric-medicine-team-training-for-animal-applications-2/">https://hyperbaricmedicine.com/courses/hyperbaric-medicine-team-training-for-animal-applications-2/</a>  They also put out white papers on training required and equipment to use during HBOT for animals.
Departments of Large Animal Clinical Sciences Pathobiology, College of Veterinary Medicine, University of Tennessee	Related to the Veterinary Hyperbaric Medicine Society
Small Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, Gainesville	Have published several articles on veterinary use of HBOT
Hyperbaric Veterinary Medicine, Boca Raton, Florida	Have published several articles on veterinary use of HBOT
Department of Integrative Physiology and Neuroscience and Graduate Program in Neuroscience, College of Veterinary Medicine, Washington State University	Have published on veterinary use of HBOT
Pet Emergency & Specialty Hospital, Thousand Oaks, CA	Have published on veterinary use of HBOT
Allegheny Veterinary Emergency Trauma and Specialty, Monroeville, PA 15146, USA. drml@aol.com	Have published on veterinary use of HBOT
Department of Veterinary and Animal Sciences and Program in Molecular and Cellular Biology,	Have published on veterinary use of HBOT, <i>at the cellular level</i>

Organization / Institution	Comments
University of Massachusetts, Amherst, Massachusetts	
Department of Veterinary Clinical Sciences, School of Veterinary Medicine, Louisiana State University, Baton Rouge	Treat animals at their clinic with HBOT protocols and publish on HBOT mechanisms

## 2. KEY PUBLICATIONS

The following table summarizes the articles identified to be the most useful, informative, or supportive of HBOT for veterinary indications, with an emphasis on trauma, thermal burns, and bites.

Table 2. HBOT-Supportive Trauma-Related Publications from Literature Review

Article Title	Indications / Key Findings	Mechanisms/Summary
Effects of hyperbaric oxygen on inflammatory response to wound and trauma: possible mechanism of action <sup>1</sup>	Wound healing	Cytokine suppression (anti-inflammatory), increase in VEGF (tissue perfusion and oxygenation)
Short duration hyperbaric oxygen treatment effects blood flow in rats: pilot observations <sup>2</sup>	Wound healing	Improve the blood flow of healing tissues, improved revascularization in the wound area
The effect of hyperbaric oxygenation on the central hemodynamics and oxygen consumption in severe mechanical trauma <sup>3</sup>	Mechanical trauma	Positive influence on hemodynamics and oxygen consumption
The efficacy of hyperbaric oxygenation in experimental and hemorrhagic shock <sup>4</sup>	Hemorrhagic Shock	Increased survival in 56 dogs when implemented early
Hyperbaric oxygen therapy. Part 1: history and principles & Part 2: application in disease <sup>5,6</sup>	Problem wounds, spinal cord injury, and cerebral ischemic injury	Increase in concentration of oxygen in plasma, increases the diffusion gradient for its delivery deeper into tissues

Article Title	Indications / Key Findings	Mechanisms/Summary
A potential role of hyperbaric oxygen exposure through intestinal nuclear factor- $\kappa$ B <sup>7</sup>	Sepsis	HBOT can modify nuclear factor- $\kappa$ B activation in intestinal mucosa and reduce nitric oxide (NO) overproduction. Consequently, bacterial translocation could decrease and sepsis risk is reduced.
Hyperbaric oxygen effects on brown recluse spider ( <i>Loxosceles reclusa</i> ) envenomation in rabbits <sup>8</sup>	Spider bite	Enhanced recovery at the histological level, reduced incidence of necrosis
Effects of hyperbaric oxygen therapy on open tibial fractures in rabbits after transient seawater immersion <sup>9</sup>	Bone fracture	Reduces inflammatory reaction, promotes osteocyte proliferation
Effect of hyperbaric oxygen treatment on incorporation of an autogenous cancellous bone graft in a nonunion diaphyseal ulnar defect in cats <sup>10</sup>	Bone graft	Median percentage of bone formation in grafted defects was significantly greater in cats given HBOT
Effects of hyperbaric oxygen treatment on healing of maxillary distraction osteogenesis in beagle dogs <sup>11</sup>	Osteogenesis	Increased blood flow
Hyperbaric Oxygen Promotes Proximal Bone Regeneration and Organized Collagen Composition during Digit Regeneration <sup>12</sup>	Wound closure and bone regeneration	Delayed blastemal deposition and better organized collagen fibers during bone formation
International Survey Regarding the Use of Rehabilitation Modalities in Horses <sup>13</sup>	Rehabilitation for injury or performance in horses	10% of survey respondents (N=305) use HBOT for horse injury or performance improvement
Effects of hyperbaric therapy on liver morphofunctional of rabbits ( <i>Oryctolagus cuniculus</i> ) after hind limb ischemia-reperfusion injury <sup>14</sup>	Prevent reperfusion injury to liver during ischemic reperfusion (post-trauma)	HBOT limits neutrophil production which reduces liver damage after reperfusion
Ischemia-reperfusion injury and hyperbaric oxygen pathways: a review of cellular mechanisms <sup>15</sup>	Ischemia-reperfusion (IR) injury following	Neutrophil clearance, reduces inflammatory response, reduces reactive oxygen species (ROS)

Article Title	Indications / Key Findings	Mechanisms/Summary
	trauma resuscitation	
The effect of combined hyperbaric oxygen and iloprost treatment on the prevention of spinal cord ischemia-reperfusion injury: an experimental study <sup>16</sup>	Preventing spinal cord ischemia-reperfusion injury	Improved neurological scores and histopathological scores
Hyperbaric oxygen treatment improves GFR in rats with ischemia/reperfusion renal injury: a possible role for the antioxidant/oxidant balance in the ischemic kidney <sup>17</sup>	Ischemic kidney injury	Improved vasodilatory response to Ach and increased regional renal blood flow
Hyperbaric oxygen reduces ischemia-induced skeletal muscle injury <sup>18</sup>	Ischemia-induced skeletal muscle injury	Reduction of changes to intracellular compounds in muscle (ATP, lactate, phosphocreatine)
The effect of hyperbaric oxygen on compromised grafts and flaps <sup>19</sup>	Enhance graft and flap survival	Decreases hypoxic insult, enhances fibroblast function and collagen synthesis, stimulates angiogenesis and inhibits ischemia-reperfusion injury
Histologic effects of hyperbaric oxygen therapy administered immediately after or two hours after ischemia-reperfusion injury: a rat abdominal skin flap model <sup>20</sup>	Skin flap survival	Thrombosis in flap microvasculature, intimal damage, edema, neutrophil infiltration, and necrosis were considerably less and neovascularization was significantly higher in HBO-treated flap tissues
The effect of hyperbaric oxygen treatment on a compromised axial pattern flap in the cat <sup>21</sup>	Pedicle skin flap healing	Skin flap color was significantly better in the treated cats on days 1, 2, and 3. The amount of exudate was significantly less in the treated cats on day 3
Hyperbaric oxygen and lymphoid system function: a review supporting possible intervention in tissue transplantation <sup>22</sup>	Preserve transplanted tissues	Suppresses autoimmune symptoms, decreases production of IL-1 and CD4 cells, and increases percentage and absolute number of CD8 cells. Improves tissue

Article Title	Indications / Key Findings	Mechanisms/Summary
		oxygenation, reduces free radical damage during reperfusion, maintains marginally ischemic tissue, and accelerates wound healing
Omental pedicle used to manage a large dorsal wound in a dog <sup>23</sup>	Necrotic wound	Healing in omental pedicle and free skin graft
Dorsal black skin necrosis in a Vietnamese pot-bellied pig <sup>24</sup>	Thermal burn / necrotic wound	Effective in both necrotic skin and fat tissue; case study only

### 3. PEER-REVIEW LITERATURE IDENTIFIED AS SUPPORTIVE OF HBOT

The following table summarizes all peer-reviewed articles identified in the search which conclude HBOT is a positive or useful therapy for veterinary purposes. Articles unrelated to trauma, burns and bites which surfaced during the literature review are also included in this table.

Table 3. All publications identified as supportive of HBOT (including and beyond trauma-related indications)

Article Title	Summary	Indication
Effect of hyperbaric oxygen treatment on incorporation of an autogenous cancellous bone graft in a nonunion diaphyseal ulnar defect in cats <sup>10</sup>	Percentage of bone formation in grafted defects was significantly greater in cats given HBOT	Incorporation of an autogenous cancellous bone graft
Hyperbaric oxygen effects on brown recluse spider ( <i>Loxosceles reclusa</i> ) envenomation in rabbits <sup>8</sup>	Histologic evaluation of wound tissue collected at euthanasia showed clear differences between rabbits receiving twice-daily HBOT treatments and those receiving daily or no treatment. The former showed complete re-epithelization or slight ulceration, while the latter usually had necrosis	Lesions from injection of brown recluse venom

Article Title	Summary	Indication
The neuroprotection effect of oxygen therapy: A systematic review and meta-analysis <sup>25</sup>	In traumatic brain injury (TBI), HBOT showed significant improvement of Glasgow outcome scale score and reduction of overall mortality	Neuroprotection in stroke and TBI
Effects of hyperbaric oxygen therapy on open tibial fractures in rabbits after transient seawater immersion <sup>9</sup>	HBOT of open tibial fractures in seawater can reduce the inflammatory reaction and reperfusion injury, and promote osteocytic proliferation and fracture healing	Bone fracture
Ischemia-reperfusion injury and hyperbaric oxygen pathways: a review of cellular mechanisms <sup>15</sup>	Pathophysiological events of IR injury are the result of reactive oxygen species (ROS) production, microvascular vasoconstriction, and ultimately endothelial cell-neutrophil adhesion with subsequent neutrophil infiltration of the affected tissue. Concluded HBO has therapeutic value	Ischemia-reperfusion (IR) injury following trauma resuscitation
The effect of combined hyperbaric oxygen and iloprost treatment on the prevention of spinal cord ischemia-reperfusion injury: an experimental study <sup>16</sup>	Neurological scores in the HBOT, IL and HBOT + IL groups were statistically significantly better compared with the control group. Histopathological scores in the HBOT, IL and HBOT + IL groups were also significantly better compared with the control group	Spinal cord ischemia-reperfusion injury
The effect of hyperbaric oxygen on compromised grafts and flaps <sup>21</sup>	HBOT can enhance graft and flap survival by several methods including decreasing the hypoxic insult, enhancing fibroblast function and collagen synthesis, stimulating angiogenesis and inhibiting ischemia-reperfusion injury	Compromised grafts or flaps, irradiated or hypoxic wound beds, excessively large harvested grafts, random flap ischemia, venous or arterial insufficiency and ischemia-reperfusion injury



Article Title	Summary	Indication
Protective effects of hyperbaric oxygen and iloprost on ischemia/reperfusion-induced lung injury in a rabbit model <sup>26</sup>	Results suggest that HBOT might be effective in prevention of lung injury after ischemia/reperfusion injury of the lower extremities	Ischemia/reperfusion-induced lung injury
Hyperbaric oxygenation alleviates MCAO-induced brain injury and reduces hydroxyl radical formation and glutamate release <sup>27</sup>	Study suggests that decreased glutamate release and reduced formation of hydroxyl free radicals might contribute to the neuroprotective effect of HBOT	Alleviates MCAO-induced brain injury
Hyperbaric oxygen treatment improves GFR in rats with ischemia/reperfusion renal injury: a possible role for the antioxidant/oxidant balance in the ischemic kidney <sup>17</sup>	HBOT reduces the decline in GFR following renal ischemia, and improves endothelial-dependent vasorelaxation, suggesting that HBOT may be beneficial in ischemic acute renal failure (ARF)	Ischemic kidney injury
Hyperbaric oxygen and lymphoid system function: a review supporting possible intervention in tissue transplantation <sup>22</sup>	Review addresses the ways HBOT may mitigate immune reactions, which are involved in rejection of allograft transplants	Preserve and protect transplanted tissues
Histologic effects of hyperbaric oxygen therapy administered immediately after or two hours after ischemia-reperfusion injury: a rat abdominal skin flap model <sup>20</sup>	HBOT was started immediately after and two hours after reperfusion in a rat model	HBOT protocol used in this study significantly increased flap survival in rat axial skin flap model
Hyperbaric oxygen reduces ischemia-induced skeletal muscle injury <sup>18</sup>	After 4 hours of ischemia, the changes in levels of the intracellular muscle compounds adenosine triphosphate, phosphocreatine, and lactate were less in HBOT rats than in untreated animals	Ischemia-induced skeletal muscle injury
Cave canem: HBO <sub>2</sub> therapy efficacy on <i>Capnocytophaga canimorsus</i> infections: a case series <sup>28</sup>	Case series on dog bites in humans	Biting injuries
Effects of hyperbaric oxygen treatment on healing of maxillary distraction osteogenesis in beagle dogs <sup>11</sup>	Blood flow in HBOT group recovered faster than in control group. Bone mineral density was higher in the HBOT group than in control group. Newly formed	Enhance the healing of distraction osteogenesis

Article Title	Summary	Indication
	bone area was larger in HBOT group than in control group.	
Hyperbaric oxygen reduces neuronal death and improves neurological outcome after canine cardiac arrest <sup>29</sup>	HBOT inhibits neuronal death and improves neurological outcome after cardiac arrest	Cerebral ischemia
The effect of hyperbaric oxygenation on the central hemodynamics and oxygen consumption in severe mechanical trauma <sup>3</sup>	Increased survival in 80 dogs with mechanical trauma	Mechanical trauma
The efficacy of hyperbaric oxygenation in experimental and hemorrhagic shock <sup>4</sup>	In 56 dogs, HBOT had large effect on hemorrhagic shock; no positive effect on traumatic shock	Hemorrhagic shock
Pressure in the treatment of spinal cord decompression sickness <sup>30</sup>	Study of 20 dogs at different pressures and oxygen percentages, treated for decompression sickness (DCS)	Decompression sickness
Oxygen in the treatment of spinal cord decompression sickness <sup>31</sup>	Study of 25 dogs at different pressures and oxygen percentages, treated for DCS	Decompression sickness
A model of spinal cord dysbarism to study delayed treatment: II. Effects of treatment <sup>32</sup>	Study of different pressures and oxygen percentages for DCS treatment	Decompression sickness
A common denominator in the etiology of adult respiratory distress syndrome <sup>33</sup>	HBO decreases energy metabolism in regions of normal circulation and in previously ischemic regions	Respiratory distress syndrome
Response of cerebrospinal fluid pressure to hyperbaric oxygenation <sup>34</sup>	Cerebrospinal fluid pressure will decrease if it is already high or increase if it started normal	Cerebrospinal fluid pressure
Pneumatosis Coli in a Dog <sup>35</sup>	Success in HBOT as treatment for gas in colonic wall	Gas in colonic wall (pneumatosis coli)
Hyperbaric oxygen and aerobic exercise in the long-term treatment of fibromyalgia: A narrative review <sup>36</sup>	Fibromyalgia, chronic pain management	Chronic pain, pain management
Effects of hyperbaric oxygen therapy on uncomplicated incisional and open wound healing in dogs <sup>37</sup>	HBOT protocol tested here was safe but did not enhance the healing of <i>uncomplicated</i> acute	Uncomplicated, open, and incisional wound healing

Article Title	Summary	Indication
	wounds and incisions in dogs, N=10	
International Survey Regarding the Use of Rehabilitation Modalities in Horses <sup>13</sup>	10% of respondents, N=305 use HBOT as a rehabilitation method for horses	Horse rehab for injury or performance issues
Safety and Tolerability of Hyperbaric Oxygen Therapy in Cats and Dogs <sup>38</sup>	78 dogs and 12 cats treated with HBOT for various indications, no major adverse events	Naturally occurring conditions
Effects of hyperbaric therapy on liver morphofunctional of rabbits ( <i>Oryctolagus cuniculus</i> ) after hind limb ischemia-reperfusion injury <sup>14</sup>	Ischemic reperfusion treated with HBOT in 4 groups of rabbits	Prevent reperfusion injury to liver during ischemic reperfusion (post-trauma)
Hyperbaric oxygenation alleviates chronic constriction injury (CCI)-induced neuropathic pain and inhibits GABAergic neuron apoptosis in the spinal cord <sup>39</sup>	Inhibitory role of HBOT in neuron apoptosis suppresses neuropathic pain	Chronic constriction injury (CCI)-induced neuropathic pain
Zoonotic necrotizing myositis caused by <i>Streptococcus equi</i> subsp. <i>Zooepidemicus</i> in a farmer <sup>40</sup>	Single human patient case study	Necrotizing soft tissue infection
Hyperbaric Oxygen Therapy in Equine Rehabilitation: Putting the Pressure on Disease <sup>41</sup>	Treatment for horses in a number of indications	Horse Rehabilitation
Hyperbaric Oxygen Promotes Proximal Bone Regeneration and Organized Collagen Composition during Digit Regeneration <sup>12</sup>	Wound closure and bone regeneration in mice	Proximal Bone Regeneration and Organized Collagen Composition during Digit Regeneration
Rectal temperature changes and oxygen toxicity in dogs treated in a monoplace chamber <sup>42</sup>	65 dogs treated for traumatic wounds and intervertebral disc disease, only a study of safety and tolerability, not effectiveness.	Traumatic wounds and intervertebral disc disease
Safety in Animal Hyperbaric Oxygen Systems <sup>43</sup>	only a study of safety and tolerability, not effectiveness	Safety only, not indications
The influences of hyperbaric oxygen therapy with a lower pressure and oxygen concentration than previous	Low pressure HBOT in dogs	Lower pressure and O <sub>2</sub> concentration than typical HBOT in dogs

Article Title	Summary	Indication
methods on physiological mechanisms in dogs <sup>44</sup>		
Dorsal black skin necrosis in a Vietnamese pot-bellied pig <sup>24</sup>	Thermal burn in a potbelly pig	Necrotic skin and fat tissue
Reduced antinociceptive responsiveness to hyperbaric oxygen in opioid-tolerant mice <sup>45</sup>	Reduced pain management in rats with substance use problems, indicates the role of opioid receptors in HBOT pain management.	Pain management
Hyperbaric oxygen therapy <sup>46</sup>	Small animal veterinary medicine	Hyperoxygenation of plasma and tissues
Beneficial effect of hyperbaric oxygen therapy on the follicular survival in the mouse ovary after transplantation <sup>47</sup>	HBOT benefit on follicular loss of ovarian tissue after transplant	Ovarian tissue transplant
Enhancement of reactive oxygen species and induction of apoptosis in streptozotocin-induced diabetic rats under hyperbaric oxygen exposure <sup>48</sup>	Diabetic rats NADPH production: oxidative stress caused by HBOT exposure induces production of ROS and apoptosis	Diabetic neuropathy
Hyperbaric oxygen therapy. Part 1: history and principles & Part 2: application in disease <sup>5,6</sup>	Review of literature for veterinary applications of HBOT	Problem wounds, spinal cord injury, and cerebral ischemic injury
Oxidative stress and gene expression of antioxidant enzymes in the streptozotocin-induced diabetic rats under hyperbaric oxygen exposure <sup>49</sup>	Diabetic rats: HBOT effect on gene expression of antioxidant enzymes: cytosolic superoxide dismutase, cytosolic glutathione peroxidase, and catalase	Diabetes associated antioxidant enzymes
Antioxidant status and lipid peroxidation in diabetic rats under hyperbaric oxygen exposure <sup>50</sup>	Diabetic rats: HBO exposure on glucose homeostasis and oxidative stress	Diabetic oxygen consumption
Enhancement of glucose toxicity by hyperbaric oxygen exposure in diabetic rats <sup>51</sup>	Oxygen toxicity and blood glucose in HBOT for diabetic rats	Diabetic oxygen consumption
Short duration hyperbaric oxygen treatment effects blood flow in rats: pilot observations <sup>9</sup>	Wound healing in rats improved with HBOT	Wound healing
Hyperbaric oxygen enhances apoptosis in hematopoietic cells <sup>52</sup>	HBOT enhances cell death of cancer cell lines	Apoptosis of cancer cells

Article Title	Summary	Indication
Omental pedicle used to manage a large dorsal wound in a dog <sup>23</sup>	Dog with necrosis on its back was treated with a skin graft and HBOT	Necrotic wound
The effect of hyperbaric oxygen treatment on a compromised axial pattern flap in the cat <sup>21</sup>	HBOT on pedicle skin flap healing in 12 cats. Skin flap color was significantly better in HBOT treated cats. The amount of exudate was significantly less in HBOT treated cats	Pedicle skin flap
Successful Healing of Tracheal Radionecrosis: Role of Hyperbaric Oxygen Therapy <sup>53</sup>	Case study with success in HBOT as component of radionecrosis management	Tracheal radionecrosis
Potential effects of hyperbaric oxygen therapy in acute pancreatitis <sup>54</sup>	HBOT improved microcirculation and anti- inflammation	Pancreatitis
Hyperbaric oxygen therapy reduces severity and improves survival in severe acute pancreatitis <sup>55</sup>	HBOT reduced severity and extent of necrosis, and improved survival in severe acute pancreatitis in 64 rats	Pancreatitis
Hyperbaric oxygen effects on tissue lesions in acute pancreatitis. Experimental study in rats <sup>56</sup>	HBOT reduced hemorrhage and acinar necrosis in 48 rats	Pancreatitis
The effects of hyperbaric oxygen on apoptosis and proliferation in severe acute pancreatitis <sup>57</sup>	HBOT may improve severe acute pancreatitis by promoting apoptosis and proliferation	Pancreatitis
Hyperbaric oxygen improves capillary morphology in severe acute pancreatitis <sup>58</sup>	HBOT normalizes pancreatic microvasculature after acute pancreatitis in 67 rats	Pancreatitis

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