



## AUTISM LITERATURE

BMC Pediatr. 2009 Mar 13;9:21.

### **Hyperbaric treatment for children with autism: a multicenter, randomized, double-blind, controlled trial.**

Rosignol DA, Rosignol LW, Smith S, Schneider C, Logerquist S, Usman A, Neubrandner J, Madren EM, Hintz G, Grushkin B, Mumper EA.

**BACKGROUND:** Several uncontrolled studies of hyperbaric treatment in children with autism have reported clinical improvements; however, this treatment has not been evaluated to date with a controlled study. We performed a multicenter, randomized, double-blind, controlled trial to assess the efficacy of hyperbaric treatment in children with autism. **METHODS:** 62 children with autism recruited from 6 centers, ages 2-7 years (mean 4.92 +/- 1.21), were randomly assigned to 40 hourly treatments of either hyperbaric treatment at 1.3 atmosphere (atm) and 24% oxygen ("treatment group", n = 33) or slightly pressurized room air at 1.03 atm and 21% oxygen ("control group", n = 29). Outcome measures included Clinical Global Impression (CGI) scale, Aberrant Behavior Checklist (ABC), and Autism Treatment Evaluation Checklist (ATEC). **RESULTS:** After 40 sessions, mean physician CGI scores significantly improved in the treatment group compared to controls in overall functioning (p = 0.0008), receptive language (p < 0.0001), social interaction (p = 0.0473), and eye contact (p = 0.0102); 9/30 children (30%) in the treatment group were rated as "very much improved" or "much improved" compared to 2/26 (8%) of controls (p = 0.0471); 24/30 (80%) in the treatment group improved compared to 10/26 (38%) of controls (p = 0.0024). Mean parental CGI scores significantly improved in the treatment group compared to controls in overall functioning (p = 0.0336), receptive language (p = 0.0168), and eye contact (p = 0.0322). On the ABC, significant improvements were observed in the treatment group in total score, irritability, stereotypy, hyperactivity, and speech (p < 0.03 for each), but not in the control group. In the treatment group compared to the control group, mean changes on the ABC total score and subscales were similar except a greater number of children improved in irritability (p = 0.0311). On the ATEC, sensory/cognitive awareness significantly improved (p = 0.0367) in the treatment group compared to the control group. Post-hoc analysis indicated that children over age 5 and children with lower initial autism severity had the most robust improvements. Hyperbaric treatment was safe and well-tolerated.

**CONCLUSION:** Children with autism who received hyperbaric treatment at 1.3 atm and 24% oxygen for 40 hourly sessions had significant improvements in overall functioning, receptive language, social interaction, eye contact, and sensory/cognitive awareness compared to children who received slightly pressurized room air.

## AUTISM LITERATURE

Epilepsy Behav. 2008 Oct;13(3):425-37. Epub 2008 Jul 31.

**A review of recent reports on autism: 1000 studies published in 2007.**

**Hughes JR.**

From 1000 studies published in 2007 on all aspects of autism, those that reached clear conclusions or included quantitative data were selected for this review. Possible etiologies include elemental metals, especially the inconsistent evidence regarding mercury from the vaccine preservative thimerosal, not used after 2001, and chromosomes and genes with the conclusion that autism has a complex genetic architecture. Also, various parental conditions are considered, as are many different abnormalities in the central nervous system, especially underconnectivity within the cortex. Furthermore, deficiencies in mirror neurons have been proposed, leading to the "theory of mind" explanation that autistic children tend to disregard others. In addition, various global deficiencies, like an increase in inhibitory synaptic transmission, are proposed. Characteristics of these children include selective (inward) attention; underresponsiveness; stereotyped repetitive motor behavior; increased head size, weight, and height; various cognitive and communicative disorders; and also epilepsy. Therapy has emphasized risperidone, but some atypical antipsychotic medications have been helpful, as have robotic aids, massage, hyperbaric oxygen, and music. Nearly every conceivable problem that a child could have can be observed in these unfortunate children.

J Med Assoc Thai. 2008 Aug;91(8):1232-8.

**Hyperbaric oxygen therapy in Thai autistic children.**

**Chungpaibulpatana J, Sumpatanarax T, Thadakul N, Chantharatreeerat C, Konkaew M, Aroonlimsawas M.**

**BACKGROUND:** Autism is a developmental and behavioral pattern, the triad of impairments, 1. social interaction, 2. social communication, 3. imagination. Their memories are seemingly in picture or photo records. Difficulties in the treatment, management, and handling of autistic children are the main problems. Hyperbaric oxygen therapy (HBOT) is a modern treatment in Thailand for nitrogen imbalance (Decompression sickness syndrome or Caisson disease). HBOT can increase plasma oxygen to the tissues including the brain. **OBJECTIVE:** To determine whether Hyperbaric Oxygen Therapy is safe to use in children with autism, and has a statistically significant effect on autistic symptoms. This is the first study in Thailand. **MATERIAL AND METHOD:** Thai Autistic children (n = 7) received HBOT (1.3 atm., 10 sessions) treatment. Assessment was done before and after treatment in five domains: Social development, Fine motor and Eye-hand coordination, Language development, Gross motor development, Self-help skills. **RESULTS:** Improvement was shown in five domains with a significant level. Seventy-five percent of children shown improvement while 25% did not seem to respond to the treatment. **CONCLUSION:** HBOT is a new treatment for Thai autistic children. Many scientific studies recently have shown that HBOT could be an effective treatment for autistic children. It could improve the major autistic symptoms.



## AUTISM LITERATURE

Med Hypotheses. 2007;68(6):1208-27. Epub 2006 Dec 4.

**Hyperbaric oxygen therapy might improve certain pathophysiological findings in autism.**

**Rossignol DA.**

Autism is a neurodevelopmental disorder currently affecting as many as 1 out of 166 children in the United States. Numerous studies of autistic individuals have revealed evidence of cerebral hypoperfusion, neuroinflammation and gastrointestinal inflammation, immune dysregulation, oxidative stress, relative mitochondrial dysfunction, neurotransmitter abnormalities, impaired detoxification of toxins, dysbiosis, and impaired production of porphyrins. Many of these findings have been correlated with core autistic symptoms. For example, cerebral hypoperfusion in autistic children has been correlated with repetitive, self-stimulatory and stereotypical behaviors, and impairments in communication, sensory perception, and social interaction. Hyperbaric oxygen therapy (HBOT) might be able to improve each of these problems in autistic individuals. Specifically, HBOT has been used with clinical success in several cerebral hypoperfusion conditions and can compensate for decreased blood flow by increasing the oxygen content of plasma and body tissues. HBOT has been reported to possess strong anti-inflammatory properties and has been shown to improve immune function. There is evidence that oxidative stress can be reduced with HBOT through the upregulation of antioxidant enzymes. HBOT can also increase the function and production of mitochondria and improve neurotransmitter abnormalities. In addition, HBOT upregulates enzymes that can help with detoxification problems specifically found in autistic children. Dysbiosis is common in autistic children and HBOT can improve this. Impaired production of porphyrins in autistic children might affect the production of heme, and HBOT might help overcome the effects of this problem. Finally, HBOT has been shown to mobilize stem cells from the bone marrow to the systemic circulation. Recent studies in humans have shown that stem cells can enter the brain and form new neurons, astrocytes, and microglia. It is expected that amelioration of these underlying pathophysiological problems through the use of HBOT will lead to improvements in autistic symptoms. Several studies on the use of HBOT in autistic children are currently underway and early results are promising.



## AUTISM LITERATURE

BMC Pediatr. 2007 Nov 16;7:36.

### **The effects of hyperbaric oxygen therapy on oxidative stress, inflammation, and symptoms in children with autism: an open-label pilot study.**

**Rossignol DA, Rossignol LW, James SJ, Melnyk S, Mumper E.**

**BACKGROUND:** Recently, hyperbaric oxygen therapy (HBOT) has increased in popularity as a treatment for autism. Numerous studies document oxidative stress and inflammation in individuals with autism; both of these conditions have demonstrated improvement with HBOT, along with enhancement of neurological function and cognitive performance. In this study, children with autism were treated with HBOT at atmospheric pressures and oxygen concentrations in current use for this condition. Changes in markers of oxidative stress and inflammation were measured. The children were evaluated to determine clinical effects and safety. **METHODS:** Eighteen children with autism, ages 3-16 years, underwent 40 hyperbaric sessions of 45 minutes duration each at either 1.5 atmospheres (atm) and 100% oxygen, or at 1.3 atm and 24% oxygen. Measurements of C-reactive protein (CRP) and markers of oxidative stress, including plasma oxidized glutathione (GSSG), were assessed by fasting blood draws collected before and after the 40 treatments. Changes in clinical symptoms, as rated by parents, were also assessed. The children were closely monitored for potential adverse effects. **RESULTS:** At the endpoint of 40 hyperbaric sessions, neither group demonstrated statistically significant changes in mean plasma GSSG levels, indicating intracellular oxidative stress appears unaffected by either regimen. A trend towards improvement in mean CRP was present in both groups; the largest improvements were observed in children with initially higher elevations in CRP. When all 18 children were pooled, a significant improvement in CRP was found ( $p = 0.021$ ). Pre- and post-parental observations indicated statistically significant improvements in both groups, including motivation, speech, and cognitive awareness ( $p < 0.05$ ). No major adverse events were observed. **CONCLUSION:** In this prospective pilot study of children with autism, HBOT at a maximum pressure of 1.5 atm with up to 100% oxygen was safe and well tolerated. HBOT did not appreciably worsen oxidative stress and significantly decreased inflammation as measured by CRP levels. Parental observations support anecdotal accounts of improvement in several domains of autism. However, since this was an open-label study, definitive statements regarding the efficacy of HBOT for the treatment of individuals with autism must await results from double-blind, controlled trials.



## AUTISM LITERATURE

Med Hypotheses. 2006;67(2):216-28. Epub 2006 Mar 22

### **Hyperbaric oxygen therapy may improve symptoms in autistic children.**

**Rossignol DA, Rossignol LW.**

Autism is a neurodevelopmental disorder that currently affects as many as 1 out of 166 children in the United States. Recent research has discovered that some autistic individuals have decreased cerebral perfusion, evidence of neuroinflammation, and increased markers of oxidative stress. Multiple independent single photon emission computed tomography (SPECT) and positron emission tomography (PET) research studies have revealed hypoperfusion to several areas of the autistic brain, most notably the temporal regions and areas specifically related to language comprehension and auditory processing. Several studies show that diminished blood flow to these areas correlates with many of the clinical features associated with autism including repetitive, self-stimulatory and stereotypical behaviors, and impairments in communication, sensory perception, and social interaction. Hyperbaric oxygen therapy (HBOT) has been used with clinical success in several cerebral hypoperfusion syndromes including cerebral palsy, fetal alcohol syndrome, closed head injury, and stroke. HBOT can compensate for decreased blood flow by increasing the oxygen content of plasma and body tissues and can even normalize oxygen levels in ischemic tissue. In addition, animal studies have shown that HBOT has potent anti-inflammatory effects and reduces oxidative stress. Furthermore, recent evidence demonstrates that HBOT mobilizes stem cells from human bone marrow, which may aid recovery in neurodegenerative diseases. Based upon these findings, it is hypothesized that HBOT will improve symptoms in autistic individuals. A retrospective case series is presented that supports this hypothesis.