



## RHEUMATOID ARTHRITIS LITERATURE

J Pain. 2007 Dec;8(12):924-30. Epub 2007 Aug 9.

**Hyperbaric oxygen treatment is comparable to acetylsalicylic acid treatment in an animal model of arthritis.**

**Wilson HD, Toepfer VE, Senapati AK, Wilson JR, Fuchs PN.**

Approximately 1 in 5 adults in the United States are affected by the pain, disability, and decreased quality of life associated with arthritis. The primary focus of treatment is on reducing joint inflammation and pain through a variety of pharmacotherapies, each of which is associated with various side effects. Hyperbaric oxygen therapy is an alternative treatment that has been recommended to treat a variety of inflammatory diseases, ranging from chronic brain injury to exercise induced muscle soreness. The purpose of this set of experiments was to explore the effect of hyperbaric oxygen therapy on joint inflammation and mechanical hyperalgesia in an animal model of arthritis, and compare these effects to treatment with aspirin.

Hyperbaric oxygen therapy significantly reduced both joint inflammation and hyperalgesia. As compared with aspirin treatment, hyperbaric treatment was equally as effective in decreasing joint inflammation and hyperalgesia. PERSPECTIVE: This article reports that hyperbaric oxygen treatment decreases pain and inflammation in an animal model of arthritis. The effect of hyperbaric oxygen treatment is very similar in magnitude to the effect of acetylsalicylic acid treatment. Potentially, hyperbaric oxygen could be used to treat pain and inflammation in patients with arthritis.

Brain Res. 2006 Jul 7;1098(1):126-8. Epub 2006 Jun 5

**Hyperbaric oxygen treatment decreases inflammation and mechanical hypersensitivity in an animal model of inflammatory pain.**

**Wilson HD, Wilson JR, Fuchs PN.**

Hyperbaric oxygen therapy has been used to treat a variety of ailments from carbon monoxide poisoning to fibromyalgia. The purpose of this experiment was to explore the effect of hyperbaric oxygen treatment on carrageenan-induced inflammation and pain in rats. Hyperbaric oxygen treatment significantly decreased inflammation and pain following carrageenan injection. Clinically hyperbaric oxygen may be used in situations where NSAIDs are contraindicated or in persistent cases of inflammation.

## RHEUMATOID ARTHRITIS LITERATURE

Z Rheumatol. 2001 Feb;60(1):1-16 **The immunologic homunculus in rheumatoid arthritis. A new viewpoint of immunopathogenesis in rheumatoid arthritis and therapeutic consequences**

**Bläss S, Engel JM, Burmester GR.**

Autoreactivity plays a major role in the pathogenesis of RA. The rheumatoid factor has been and still is for now more than 50 years the only autoreactivity that is clinically applied in the diagnosis of RA. This well reflects the current way of thinking that a single antigen or a single cause drives an individual into disease. Although by now many other autoantigens and autoreactivities have been described, their discovery was always on the search for the one and only autoreactivity that causes RA. This includes also immune reactivities directed against xenogenic antigens. But, none of the known RA-associated autoreactivities is present in all RA patients and none of them occurs exclusively in RA. Thus, the observed sensitivities and specificities are well below 100%. Therefore, RA has often been postulated to consist of various immunological subentities with similar clinical symptoms. Nevertheless, none of the autoreactivities correlates with a distinct clinical feature or course of disease. It is about time to say goodbye to the idea that a single antigen or immunoreactivity causes and maintains rheumatoid arthritis. In this paper we present RA as the clinical outcome of an immune system that has shifted from a healthy to an autoimmune steady state. This is accomplished by many different reactivities and autoreactivities that occur either in parallel or one after the other. The entirety of the known RA-associated reactivities and (auto)antigens is presented in detail. The major RA-relevant autoantigens comprise BiP, citrulline, the Sa-antigen, hnRNP A2, p205, IgG, calpastatin, calreticulin, collagen and the shared HLA-DR epitope. The accumulation of factor--involving autoreactivities, cytokines, environmental and genetic factors--that challenge the normal regulatory mechanisms of the immune system lead to a regulatory catastrophe. In individuals developing the clinical features of RA the immune system has been regulated to a new--autoimmune--steady state. This attractor "rheumatoid arthritis" has many features of what has originally been described by Irun Cohen as the immunological homunculus: The healthy immune system is configured such as to direct its attention to major self-antigens. Thus it creates an autoreactivity to many autoantigens as a prerequisite for regulatory mechanisms that are sufficient to control them. The shift from the normal to rheumatoid attractor involves the inflammatory cytokines TNF-alpha, IL-1 and IL-6, autoreactive T- and B cells directed at a variety of synovial and macrophages, tissue destruction and genetic factors such as the association with shared epitope. Environmental factors involved may also, but do not necessarily, include infection. With the appearance of clinical features of RA, naive, potentially autoreactive T cells infiltrate the synovial compartment and become activated by dendritic cells and other APCs. The autoantigenic peptides that are presented to these T cells are derived from inflammatory cell and tissue destruction as well as from tissue repair and remodeling processes. These T cells proliferate and either provide help to B cells with the specificity to the same antigens or cause direct cytopathic tissue damage. Thereby, more and novel antigens are generated, released and presented again to naive or primed autoreactive T cells. These processes involving cytokines, tissue destruction and autoreactive T cells are sufficient to maintain RA even without the permanent presence of a triggering agent. The recursive autoimmune processes are well consistent with the finding of the many different autoreactivities in RA and their respective sensitivities and specificities. The massive influx of T cells into the arthritic joint is accompanied by the anergization of over 90% of T cells in this compartment--which further substantiates the concept of the RA attractor within the self-regulating immune system. Thereby, the RA-attracted

## RHEUMATOID ARTHRITIS LITERATURE

immune system is not able to completely downregulate the inflammation and the local tissue damage/repair. Thus, the immune system is permanently stimulated and suddenly by chance shifts to a stable state different from the healthy system--reaching the wide fields of rheumatoid arthritis which in itself is self-sustaining as the healthy state before disease onset.

Int J Dermatol. 1992 Aug;31(8):594-6

### **Pyoderma gangrenosum treated with hyperbaric oxygen therapy.**

**Wasserteil V, Bruce S, Sessoms SL, Guntupalli KK.**

The management of pyoderma gangrenosum often requires systemic drug therapy, such as corticosteroids, sulfones, or immunosuppressants, either alone or in combination. Inconsistent response to therapy is a source of frustration to both patient and physician. Several reports in the literature document the successful treatment of pyoderma gangrenosum with hyperbaric oxygen therapy. In our patient, a woman with severe rheumatoid arthritis and diabetes mellitus, hyperbaric oxygen therapy not only promoted healing of pyoderma gangrenosum but permitted reduction of systemic corticosteroids.

Fiziol Zh. 1991 Sep-Oct;37(5):55-60

### **Hyperbaric oxygenation in the comprehensive therapy of patients with with rheumatoid arthritis (clinico-immunologic study)**

**Lukich VL, Poliakova LV, Sotnikova TI, Belokrinitskii DV.**

For 35 of 50 patients with rheumatoid arthritis traditional drug therapy was a minor success for a long time. Without any modifications of the drug therapy every patient went through a course of hyperbaric oxygenation (HBO): 21 sessions under 1.7 ATA for 40 min. Good clinical results both immediate and remote have been obtained. The effect of HBO on the immune system of the patients has intensified the suppressive function of T-lymphocytes (especially with systemic symptoms of the disease), normalized cell-bound immunity and decreased the serum concentration in immune complexes.

Nippon Seikeigeka Gakkai Zasshi. 1985 Jan;59(1):17-26

### **Superoxide dismutase and hyperbaric oxygen therapy of the patient with rheumatoid arthritis**

**Kamada T.**

Cu, Zn-SOD values were measured by enzyme immunoassay in the synovial fluid, leukocytes in the synovial fluid, synovial membrane, and leukocytes in blood of the patients with rheumatoid arthritis. SOD activity, lipoperoxide value in serum, ESR, and Lansbury's index of the patients with rheumatoid arthritis under hyperbaric oxygen (HBO) therapy were also investigated. SOD values of synovial fluid and of leukocytes in synovial fluid from rheumatoid arthritis group were found to be higher than those from osteoarthritis group. No significant difference was found the SOD values in leukocytes of blood and synovial membrane between two groups. In the patients with rheumatoid arthritis under HBO therapy the SOD activity was increased, whereas lipoperoxide values was decreased. Furthermore, ESR and Lansbury's index showed a remarkable recovery. These results suggest that HBO therapy may be an effective treatment for the patients with rheumatoid arthritis.



## RHEUMATOID ARTHRITIS LITERATURE

Clin Orthop Relat Res. 1982 Jan-Feb;(162):282-7.

**A remarkable increase of superoxide dismutase activity in synovial fluid of patients with rheumatoid arthritis.**

**Igari T, Kaneda H, Horiuchi S, Ono S.**

Superoxide dismutase activities in the synovial fluid of patients with rheumatoid arthritis and osteoarthritis were determined by the technique of McCord and Fridovich. The superoxide dismutase activity from the rheumatoid arthritis group was found to be remarkably higher than that from the osteoarthritis group. The high superoxide dismutase activity of rheumatoid arthritis is correlated with the severity of the disease. A significant correlation was also found between C-reactive protein and superoxide dismutase activity. These observations suggest that superoxide dismutase activity is a manifestation of the acute inflammatory stage of rheumatoid arthritis.