Town & Country
Compounding and Consultation
"Customized, Patient Specific, Compounded Medications"

Low Dose Naltrexone and Autoimmune Disease

FDA-approved naltrexone, in a low dose, **can boost the immune system — helping those with HIV/AIDS, cancer, autoimmune diseases, and central nervous system disorders**

In Brief

There is growing recognition in the scientific community that autoimmune diseases result from immunodeficiency, which disturbs the ability of the immune system to distinguish "self" from "non-self". The normalization of the immune system induced by LDN makes it an obvious candidate for a treatment plan in such diseases.

The experience of people who have autoimmune diseases and who have begun LDN treatment has been remarkable. Patients with diagnoses such as systemic lupus, rheumatoid arthritis, Behcet's syndrome, Wegener's granulomatosis, bullous pemphigoid, psoriasis, and Crohn's disease have all benefited.

Because LDN clearly halts progression in multiple sclerosis, its use has been more recently extended to other neurodegenerative diseases, such as Parkinson's disease and amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease) whose etiology remains unknown but for which there is suggestive evidence of a possible autoimmune mechanism.

In addition, people with fibromyalgia and chronic fatigue syndrome have had marked improvement using LDN, suggesting that these entities probably have an important autoimmune dynamic as well.

Source: www.lowdosenaltrexone.org www.ldninfo.org

Recent Developments

> Parkinson's Disease

As of September 2003, Dr. Bihari reported that there were seven patients with Parkinson's Disease (PD) in his practice, all of whom have shown no progression since beginning LDN. Indeed, two of them have shown clear evidence of improvement in signs and symptoms.

Two people with PD, the first patients with that disorder known to have been treated with LDN, have had good results that persist after more than two years on LDN. One patient, a man in his mid-60's from New Jersey, had his first annual revisit to Dr. Bihari for a check-up in April 2002. His wife reported that, in contrast to all the other members of his PD monthly group meeting, he seemed to have shown no deterioration in his functional abilities throughout the prior year. On a thorough neurological examination, Dr. Bihari found improvement in some signs of his Parkinson's Disease. Among these was now the absence of the glabellar sign, a primitive reflex that is consistently found in those with PD and which the patient had demonstrated the year before on his initial examination.

Another patient with PD is a 48-year-old male who began LDN in December 2000. Because he was seeing no improvement in his condition (although he wasn't getting any worse), he discontinued LDN in early March 2002. He called Bihari in mid-May 2002 because he was now beginning to see, for the first time in over a year, worsening of his PD symptoms. In those three months, the disease manifested increased tremor and rigidity in the involved arm. He resumed LDN and over the following two months experienced reversal of the progression that had occurred off of the drug. He was also able to reduce his dopamine-analogue medication by two-thirds, relieving the depression that it was producing.

> Amyotrophic Lateral Sclerosis

In the spring of 2002, several people with amyotrophic lateral sclerosis, after reading the material about multiple sclerosis on this website, asked their physicians to prescribe LDN for their ALS. Two patients with advanced disease showed significant improvement in their breathing, as measured by a forced vital capacity (FVC). One had a 25% improvement within two months of beginning LDN and the other 11% improvement. A third patient who also has advanced ALS and an impaired FVC has had significant subjective improvement in his ability to breathe and a reduction in his resting pulse from 96 to the low 80's.

Subsequently, in early fall 2002, the first patient, who had been taking only 3mg of LDN nightly, notified us that both his FVC and that of the second patient, who was using the 4.5mg dose, had reverted to their usual baseline capacities, but that their FVC's appeared to be remaining stable for a prolonged period.

[Ed. Note: Given the repeated demonstration of LDN's efficacy in halting progression in virtually all cases of MS (see LDN and MS), and the possibility of its having a therapeutic effect in Parkinson's Disease and in ALS, it may be timely to consider LDN in treating the full spectrum of neurodegenerative diseases whose etiology is unknown—all of which may well have a significant underpinning of immunodeficiency/autoimmunity causing their neurological syndromes. Alzheimer's disease also suggests itself as an important possibility.]

Noteworthy Cases

> Wegener's Granulomatosis

D. is a 62-year-old male. In February 2000, after 3 years of recurrent upper respiratory symptoms and cough, and more recent difficulty with vision, he was admitted to a Boston medical center because of suspected vasculitis. He had lost energy and could not walk more than ten to fifteen steps without having to rest. The autoimmune disease Wegener's granulomatosis was considered probable, due to an elevated sedimentation rate (80) and a positive Anti-Neutrophil Cytoplasmic Antibody [ANCA] level of 65. In May 2000, nasal tissue removed at surgery confirmed "necrotizing vasculitis *… highly suggestive of Wegener's* granulomatosis." He was treated with corticosteroids for nine months, until January 2001. The ANCA test was 1.9 in July 2000, 12 in January 2001 and back up to 40 in May 2001, at which time he was experiencing marked fatigue and upper respiratory symptoms.

D. started using low dose naltrexone (4.5mg) nightly in mid-May 2001. After several weeks he noticed a decrease in congestion and a noticeable increase in overall energy. Subsequent tests of ANCA were 16 in August 2001 and the most recent test of ANCA in late December 2001 was down to 1.0. As of September 2002, he continues to report a high energy level—equal to that prior to disease onset—and he is enjoying his noticeable improvement in overall health.

> Crohn's Disease

As of September 2002, Dr. Bihari was following eight patients with Crohn's Disease on LDN. In all eight cases, within 14-21 days the signs and symptoms of disease activity stopped. All eight had remained stable since anywhere from 2 months to 36 months.

106 Prospect Street, Ridgewood, NJ 07450 Ofc: 201-447-2020 Fax: 201-447-3253
www.tccompound.com tompellegrino@tccompound.com

> Rheumatoid Arthritis

Ten patients with this disease have been treated with LDN in recent years. In all ten patients the joint pain and swelling cleared, in some, leaving residual joint distortion. Two of the patients stopped LDN for several weeks because of travel. Both had an immediate exacerbation. One patient who was responding well on LDN had a mild exacerbation during a period of severe marital stress.

> Pemphigoid

K. is an 82-year-old woman who, over a period of three months, developed blisters on her ankles, the soles of her feet, her arms and her neck, which on biopsy proved to be pemphigoid. She was referred to a dermatologist specializing in this disease who treated her with prednisone 40 mg/day, which slowed disease progression but did not clear her blisters. When LDN was added by Dr. Bihari, her blisters cleared and slowly healed over a 6-week period, during which time she slowly tapered her prednisone. On her last visit, she was on both LDN each night and prednisone 5mg every other day with no exacerbation.

NALTREXONE Background

Naltrexone was licensed in 1984 by the FDA in a 50 mg dose as a treatmen for heroin addiction. It is a pure opiate antagonist (blocking agent) and its purpose was to block the opioid receptors that heroin acts on in the brain. When it was licensed, Dr. Bihari, then involved in running programs for treating addiction, tried it in more than 50 heroin addicts who had stopped heroin use. None of the patients would stay on the drug because of side effects experienced at 50 mg such as insomnia, depression, irritability and loss of feelings of pleasure, all due to the effect of the drug at this dose in blocking endorphins. These are the hormones in the body that heroin resembles. Physicians treating heroin addicts therefore, for the most part, stopped prescribing naltrexone. In 1985, a large number of heroin addicts began to get sick with AIDS—studies showed that 50% of heroin addicts were HIV Positive.

Dr. Bihari and his colleagues decided to shift their research focus to AIDS, in particular focusing on ways of strengthening the immune system. Since endorphins are the hormones centrally involved in supporting and regulating the immune system, levels of endorphins were measured in the blood of AIDS patients. They were found to average only 25% of normal.

Naltrexone, when given to mice and people at high doses, raises endorphin levels in the body's effort to overcome the naltrexone blockade. This drug became the focus of Dr. Bihari's research group. When the group discovered that endorphins are almost all produced in the middle of the night, between 2 AM and 4 AM, the studies focused on small doses (1.5-4.5 mg at bedtime) with the hope that a brief period of endorphin blockade before 2 AM might induce an increase in the body's endorphin production. In fact, the drug did so in this dosage range. It had no effect below 1.5 mg and too much endorphin blockade at doses over 5 mg. A placebo-controlled trial in AIDS patients showed a markedly better outcome in patients on the drug as compared with those on placebo.

During the trial, a close friend of Dr. Bihari's daughter had three acute episodes of multiple sclerosis over a nine-month period with complete spontaneous recovery from each. Because of his knowledge of MS as a neurologist and of recent evidence of an autoimmune component in the disease, Dr. Bihari started his daughter's friend on naltrexone at 3 mg every night at bedtime. She took it for five years with no further attacks. At that point, when a particular month's supply ran out, she stopped it because of some denial that she had MS. Three and a half weeks later, she developed an episode of weakness, numbness, stiffness and spasms in her left arm and resumed LDN, which she has stayed on since. This episode cleared and over the 12 years since, she has had no further disease activity.

The apparent mechanism of action of LDN in this disease parallels that in AIDS and other immune-related diseases. A small dose of the drug taken nightly at bedtime doubles or triples the endorphin levels in the body all of the next day restoring levels to normal. Since endorphin levels are low in people with MS, immune function is poorly orchestrated with significant impairment of the normal immune supervisory function of CD4 cells. In the absence of normal orchestration of immune function, some of the immune system cells "forget" their genetically determined ability to distinguish between the body's 100,000 unique chemical structures (called "self") and the chemical structures of bacteria, fungi, parasites and cancer cells (called "non-self"). With this loss of immunologic memory, some cells begin to attack some of the body's unique chemical structures. In the case of people with MS, the tissue attacked by immune cells (particularly macrophages) is primarily the myelin that insulates nerve fibers. These attacks result in scars in the brain and spinal cord called plaques. LDN in such patients works by restoring endorphin levels to normal, thereby allowing the immune system to resume its normal supervision and orchestration.

There exists a common notion that the immune system in a person with an autoimmune disorder is too strong and, in its exuberance, targets a body tissue for attack. Rather, the evidence is more consistent with autoimmunity resulting from immunodeficiency.[1] Kukreja et al have demonstrated that multiple immunoregulatory T cell defects lie behind Type 1 diabetes both in humans and in non-obese diabetic mice.[2]

Multiple scientific papers from various other research centers have demonstrated that an underlying immunodeficiency is characteristic of any tested autoimmune disease. Examples thus far reported include multiple sclerosis, rheumatoid arthritis, Crohn's disease, and chronic fatigue syndrome.[3, 4, 5]

Sacerdote et al measured low beta-endorphin levels in two animal examples of autoimmune disease — a mouse strain with a lupus-like syndrome and a strain of chicken with an autoimmune thyroiditis.[6] They had significantly lower hypothalamic concentrations of the opioid than normal controls. In each case, the low levels of beta-endorphin were found well before the expression of autoimmune disease. This adds to considerable evidence of a key role for endorphins in regulating immune responses and suggests a therapeutic pathway.

Bihari et al found that a low oral dose of the opioid antagonist naltrexone, when taken at bedtime, led to a doubling or tripling of low levels of circulating beta-endorphin.[7] Bihari has since treated some 100 people with autoimmune disorders. None of them has progressed further while the patient continued taking low dose naltrexone each night at bedtime. Since no side effects are apparently associated with its use, this medication might well be studied as a possible preventive for Type I diabetes in those youngsters with beta-cell autoantibodies.

Footnotes

1. *Buckley RH. Primary Immunodeficiency Diseases Due to Defects in Lymphocytes. N Engl J Med. 2000; 343:1313-1324.*
2. *Kukreja A, Cost G, Marker J, et al. Multiple immuno-regulatory defects in type-1 diabetes. J Clin Invest. 2002;109(1):131-40.*
3. *Thewissen M, Linsen L, Somers V, Geusens P, Raus J, Stinissen P. Premature immunosenescence in rheumatoid arthritis and multiple sclerosis patients. Ann N Y Acad Sci. Jun 2005;1051: 255-62.*
4. *Marks DJ, Harbord MW, MacAllister R, Rahman FZ, Young J, Al-Lazikani B, Lees W, Novelli M, Bloom S, Segal AW. Defective acute inflammation in Crohn's disease: a clinical investigation. Lancet. Feb 2006;367 (9511): 668-78.*
5. *Vernon SD, Reeves WC. The challenge of integrating disparate high-content data: epidemiological, clinical and laboratory data collected during an in-hospital study of chronic fatigue syndrome. Pharmacogenomics. Apr 2006;7 (3): 345-54.*
6. *Sacerdote P, Lechner O, Sidman C, et al. Hypothalamic beta-endorphin concentrations are decreased in animals models of autoimmune disease. J Neuroimmunol. 1999;97(1-2):129-33.*
7. *Bihari B, Drury FM, Ragone VP, et al. Low Dose Naltrexone in the Treatment of Acquired Immune Deficiency Syndrome. Oral Presentation at the IV International AIDS Conference, Stockholm, Jun 1988.*

106 Prospect Street, Ridgewood, NJ 07450 Ofc: 201-447-2020 Fax: 201-447-3253

www.tccompound.com tompellegrino@tccompound.com