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What is low-dose naltrexone and why is it important?

> Low-dose naltrexone holds great promise for the millions of people worldwide with autoimmune diseases or central nervous system disorders or who face a deadly cancer.

Naltrexone itself was approved by the FDA in 1984 in a 50mg dose for the purpose of helping heroin or opium addicts, by blocking the effect of such drugs. By blocking opioid receptors, naltrexone also blocks the reception of the opioid hormones that our brain and adrenal glands produce: beta-endorphin and met-enkephalin. Many body tissues have receptors for these endorphins and enkephalins, including virtually every cell of the body's immune system.

In 1985, [Bernard Bihari, MD](#), a neurologist from Harvard Medical School with a clinical practice in New York City, discovered the effects of a much smaller dose of naltrexone (approximately 3mg once a day) on the body's immune system. He found that this low dose, taken at bedtime, was able to enhance a patient's response to infection by HIV, the virus that causes AIDS. [Note: Subsequently, the optimal adult dosage of LDN has been found to be 4.5mg.]

In the mid-1990's, Dr. Bihari found that patients in his practice with cancer (such as lymphoma or pancreatic cancer) could benefit, in some cases dramatically, from LDN. In addition, people who had an autoimmune disease (such as lupus) often showed prompt control of disease activity while taking LDN.

How does LDN work?

> LDN boosts the immune system, activating the body's own natural defenses.

Up to the present time, the question of "What controls the immune system?" has not been present in the curricula of medical colleges and the issue has not formed a part of the received wisdom of practicing physicians. Nonetheless, a body of research over the past two decades has pointed repeatedly to one's own endorphin secretions (our internal opioids) as playing the central role in the beneficial orchestration of the immune system, and recognition of the facts is growing.

Witness these statements from a review article of medical progress in the [November 13, 2003 issue of the prestigious New England Journal of Medicine](#): "Opioid-Induced Immune Modulation: Preclinical evidence indicates overwhelmingly that opioids alter the development, differentiation, and function of immune cells, and that both innate and adaptive systems are affected.

Bone marrow progenitor cells, macrophages, natural killer cells, immature thymocytes and T cells, and B cells are all involved. The relatively recent identification of opioid-related receptors on immune cells makes it even more likely that opioids [have direct effects on the immune system](#). There is also [epidemiological evidence](#) that chronic opiate users have a higher frequency and higher severity of infections compared to the normal population.

Most opioids used in clinical pain management [has been shown to have immunomodulatory effects](#) and these effects are independent of their antinociceptive properties and appear to be related to the molecular structure of the opioid. Some opioids (morphine, fentanyl, methadone, codeine) are more immunosuppressive than others (hydromorphone, tramadol, hydrocodone, and oxycodone (Oxynorm and Oxycontin). Buprenorphine (Temgesic) produces little or no negative immune alterations and may enhance immune function. Antagonists at the OP3 receptor as naltrexone and endorphins like enkephalin and met-enkephalin also appear to enhance immune function.

The brief blockade of opioid receptors between 2 a.m. and 4 a.m. that is caused by taking LDN at bedtime each night is believed to produce a prolonged up-regulation of vital elements of the immune system by causing an increase in endorphin and enkephalin production. Normal volunteers who have taken LDN in this fashion have been found to have much higher levels of beta-endorphins circulating in their blood in the following days. Animal research by [I. Zagon, PhD](#), and his colleagues has shown a marked increase in met-enkephalin levels as well. [Note: Additional information for Dr. Zagon can be found at the end of this page.]

Bihari says that his patients with HIV/AIDS who regularly took LDN before the availability of HAART were generally spared any deterioration of their important helper T cells (CD4+).

In human cancer, research by Zagon over many years has demonstrated inhibition of a number of different human tumors in laboratory studies by using endorphins and low dose naltrexone. It is suggested that the increased endorphin and enkephalin levels, induced by LDN, work directly on the tumors' opioid receptors — and, perhaps, induce cancer cell death (apoptosis). In addition, it is believed that they act to increase natural killer cells and other healthy immune defenses against cancer.

In general, in people with diseases that are partially or largely triggered by a deficiency of endorphins (including cancer and autoimmune diseases), or are accelerated by a deficiency of endorphins (such as HIV/AIDS), restoration of the body's normal production of endorphins is the major therapeutic action of LDN.

What diseases has it been useful for and how effective is it?

> **Bernard Bihari, MD, as well as other physicians and researchers, have described beneficial effects of LDN on a variety of diseases:**

Cancers:

- Bladder Cancer
- Breast Cancer
- Carcinoid
- Colon & Rectal Cancer
- Glioblastoma
- Liver Cancer
- Lung Cancer (Non-Small Cell)
- Lymphocytic Leukemia (chronic)
- Lymphoma (Hodgkin's and Non-Hodgkin's)
- Malignant Melanoma
- Multiple Myeloma
- Neuroblastoma
- Ovarian Cancer
- Pancreatic Cancer
- Prostate Cancer (untreated)
- Renal Cell Carcinoma
- Throat Cancer
- Uterine Cancer

Other Diseases:

- ALS (Lou Gehrig's Disease)
- Alzheimer's Disease
- Ankylosing Spondylitis
- Autism Spectrum Disorders
- Behcet's Disease
- Celiac Disease
- Chronic Fatigue Syndrome
- CREST syndrome
- Crohn's Disease
- Dermatomyositis
- Emphysema (COPD)
- Endometriosis
- Fibromyalgia
- HIV/AIDS
- Irritable Bowel Syndrome (IBS)
- Multiple Sclerosis (MS)
- Parkinson's Disease
- Pemphigoid
- Primary Lateral Sclerosis (PLS)
- Psoriasis
- Rheumatoid Arthritis
- Sarcoidosis
- Scleroderma
- Stiff Person Syndrome (SPS)
- Systemic Lupus (SLE)
- Transverse Myelitis
- Ulcerative Colitis
- Wegener's Granulomatosis

> LDN has demonstrated efficacy in thousands of cases.

Cancer. As of mid-2004, Dr. Bihari reported having treated over 300 patients who had a cancer that had failed to respond to standard treatments. Of that group, some 50%, after four to six months treatment with LDN, began to demonstrate a halt in cancer growth and, of those, over one-third have shown objective signs of tumor shrinkage.

Autoimmune diseases. Within the group of patients who presented with an autoimmune disease (see above list), almost none have failed to respond to LDN according to Dr Biharis group; Almost all have experienced a halt in progression of their illness. In many patients there was a marked remission in signs and symptoms of the disease. The greatest number of patients within the autoimmune group are people with multiple sclerosis, of whom there were some 400 in Dr. Bihari's practice. Less than 1% of these patients have ever experienced a fresh attack of MS while they maintained their regular LDN nightly therapy.

In 2010, two randomized placebo-controlled studies on the use of LDN for MS showing conflicting results. One [placebo-controlled cross-over study](#) from Iran showed no significant effect, while another [placebo controlled study from the US](#) showed excellent effects.

HIV/AIDS. As of September 2003, Dr. Bihari had been treating 350 AIDS patients using LDN in conjunction with accepted AIDS therapies. Over the prior 7 years over 85% of these patients showed no detectable levels of the HIV virus — a much higher success rate than most current AIDS treatments, and with no significant side effects. It is also worth noting that many HIV/AIDS patients have been living symptom-free for years taking only LDN with no other medications.

Central Nervous System disorders. Anecdotal reports continue to be received concerning beneficial effects of LDN on the course of Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerosis (ALS—Lou Gehrig's disease), and primary lateral sclerosis. [Dr. Jaquelyn McCandless](#) has found a very positive effect of LDN, in appropriately reduced dosage and applied as a transdermal cream, in children with autism.

> How is it possible that one medication can impact such a wide range of disorders?

The disorders listed above all share a particular feature: in all of them, the immune system plays a central role. Low blood levels of endorphins are generally present, contributing to the disease-associated immune deficiencies.

Research by others — on neuropeptide receptors expressed by various human tumors — has found opioid receptors in many types of cancer:

- Brain tumors (both astrocytoma and glioblastoma)
- Breast cancer
- Endometrial cancer
- Head and neck squamous cell carcinoma
- Myeloid leukemia
- Lung cancer (both small cell and non-small cell)
- Neuroblastoma and others...

These findings suggest the possibility for a beneficial LDN effect in a wide variety of common cancers.

> LDN can be prescribed by your doctor, and should be prepared by a reliable compounding pharmacy.

Naltrexone is a prescription drug, so your physician would have to give you a prescription after deciding that LDN appears appropriate for you.

> Side effects:

LDN has virtually no side effects. Occasionally, during the first week's use of LDN, patients may complain of some difficulty sleeping. This rarely persists after the first week. Should it do so, dosage can be reduced from 4.5mg to 3mg nightly.

> Cautionary warnings:

1. Because LDN blocks opioid receptors throughout the body for three or four hours, people using medicine that is an opioid agonist, i.e. narcotic medication — such as Ultram (tramadol), morphine, Percocet, Duragesic patch or codeine-containing medication — should not take LDN until such medicine is completely out of one's system. Patients who have become dependant on daily use of narcotic-containing pain medication may require 10 days to 2 weeks of slowly weaning off of such drugs entirely (while first substituting full doses of non-narcotic pain medications) before being able to begin LDN safely.

2. Those patients who are taking thyroid hormone replacement for a diagnosis of Hashimoto's thyroiditis with *hypothyroidism* ought to begin LDN at the lowest range (1.5mg for an adult). Be aware that LDN may lead to a prompt decrease in the autoimmune disorder, which then may require a rapid reduction in the dose of thyroid hormone replacement in order to avoid symptoms of *hyperthyroidism*.
3. Full-dose naltrexone (50mg) carries a cautionary warning against its use in those with liver disease. This warning was placed because of adverse liver effects that were found in experiments involving 300mg daily. The 50mg dose does not apparently produce impairment of liver function nor, of course, do the much smaller 3mg and 4.5mg doses.
4. People who have received organ transplants and who therefore are taking immunosuppressive medication on a permanent basis are cautioned against the use of LDN because it may act to counter the effect of those medications.

Ultra-Low.Dose Naltrexone:

Physical dependence or withdrawal is an expected effect of prolonged opioid therapy. Oxytrex (oxycodone + ultralow-dose naltrexone) is an investigational drug shown here to minimize physical dependence while providing strong analgesia with twice-daily dosing. [In a 719-patient, double-blind, placebo- and active-controlled Phase III clinical trial](#) in chronic low back pain, patients were randomized to receive placebo, oxycodone qid, or oxytrex qid or bid. Each oxytrex tablet contains 1 microg naltrexone. Active treatment groups attained comparable analgesia despite significantly lower drug use ($P = .03$) by oxytrex patients. Patients taking oxytrex bid reported 55% less physical dependence than patients on oxycodone ($P = .01$) Previous clinical data have shown ultralow-dose naltrexone enhances and prolongs oxycodone analgesia, and preclinical data also show a suppression of opioid tolerance and dependence. A cellular mechanism of action has been demonstrated to be the prevention of aberrant G protein signalling by mu opioid receptors caused by chronic opioid administration.

References:

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6. [Low-dose naltrexone therapy improves active Crohn's disease.](#)

7. [Low-dose naltrexone for the treatment of irritable bowel syndrome: a pilot study.](#)
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