

# LDN in Allergies, Autoimmune Disease and Pediatrics

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I am both a physician prescribing and a patient  
taking LDN

# LDN Basics

- LDN blocks opioid receptors for a few hours while you're sleeping.
- This results in up regulation of your body's ability to make and use endorphins.
- Endorphins control the immune and endocrine system.
- Think second grade teacher...

# A Simple Analogy

Teacher Leaves

- chaos: color on the desks, make origami out of their work books, finger paint the walls

Teacher Returns

- diverted from from their rambunctious tendencies and directed to appropriate tasks

Endorphins as Teachers

- direct your immune system as to the correct mode of behavior and redirect bad behavior

# Heat Shock Proteins: Linking

## • Autoimmunity & Allergies

Allergic and autoimmune diseases are forms of altered immune responses directed respectively against exogenous and endogenous antigens. A growing body of experimental evidence exists to support a common pathogenetic link between allergy and autoimmunity... HSPs have been recognized as antigens in autoimmune diseases and also as the main proteins of environmental allergens.

- Heat Shock Protein-derived peptides.... Medline article

# Autoimmune Triggers

- Environmental toxins & Dietary factors
- Stress
- Endocrine dysfunction including Male/female hormones, thyroid, adrenals, HPA
- Sleep deprivation
- Infectious agents
- Allergens
- Genetics

# Asthma and Allergy Triggers & Contributors

- Environmental Toxins
- Infectious agents
- Dietary Factors
- Endocrine dysfunction
- Stress
- Lack of Sleep
- Genetics

# Complex Interactions


- A model of interactions between the initiating factors (susceptibility genes/environmental stimuli) and the modulating factors (sex hormones/neuroendocrine influences) has been proposed in the progression of the autoimmune diseases.
- Faith; Robert E.; Faith, Robert E.; Murgu, Anthony J.; Good, Robert A.; Plotnikoff, Nicholas P. (2012-05-07). Cytokines: Stress and Immunity, Second Edition (Page 363). CRC Press. Kindle Edition.

# Cascade caused by Triggers

Activation of the hypothalamic--pituitary--adrenal (HPA) axis

A light blue arrow pointing downwards from the first box to the second box.

Release of glucocorticoids and stimulation of the sympathetic nervous system

A light blue arrow pointing downwards from the second box to the third box.

Epinephrin and Norepinephrine release and mobilization of endogenous opoid peptides



# Opioids Act On All Your Cells

- Recognition of a role for the opioid peptides in the modulation of the immune response is of particular importance. These substances act directly upon specific opioid receptors present in practically all cellular types implicated in the immune response, including lymphocytes B and T, natural killer (NK) cells, monocytes, macrophages, and neutrophils.
- Lymphocytes may also synthesize these peptides, allowing for the action of these substances at different levels because they are present in circulation and may migrate toward areas of need. In fact, this peptide–immune cell interaction appears to engage wide participation of the innate and specific immune responses.
- Faith; Robert E.; Faith, Robert E.; Murgu, Anthony J.; Good, Robert A.; Plotnikoff, Nicholas P. (2012-05-07). Cytokines: Stress and Immunity, Second Edition (Page 126). CRC Press. Kindle Edition.

# The Effects of Opioids

- Increases inflammatory cytokines
- Disrupts the HPA axis
- Significantly impairs and has an inhibitory effect on an individual's immune system
- Stimulates tumor cell growth
- Inhibits the healing functions of the body
- Produces vulnerability to infection

# Hormone Imbalance

- The association between a blunted HPA axis and susceptibility to autoimmune/inflammatory disease has been clearly shown in many animal models, across species, strains, and diseases.
- Sternberg, E.M., Neuroendocrine regulation of autoimmune/inflammatory disease, J Endocrinol., 169, 429, 2001.

# Hormones and Immune Health

- Sex hormones directly affect immune mechanisms, including the homing of lymphocytes, the expression of adhesion molecules, the balance between Th1 and Th2 responses, the transcription and translation of cytokine genes, antigen presentation and costimulation, and T cell receptor signaling.
- Faith; Robert E.; Faith, Robert E.; Murgu, Anthony J.; Good, Robert A.; Plotnikoff, Nicholas P. (2012-05-07). Cytokines: Stress and Immunity, Second Edition (Page 362). CRC Press. Kindle Edition.

# Asthma & Airborne

## Allergies

- TH2 inflammatory cytokines (CD3, CD4, CD5, CD9, CD13), considered to be the primary mechanism underlying asthma & allergies
- Increased and abnormal cytokines in the airways is the primary treatment goal of corticosteroids
- Granulocyte-macrophage colony-stimulating factor recruits, mobilizes and activates eosinophils for subsequent mucosal damage
- IgE activation triggers release of histamine and leukotrienes which produce symptoms

# Exorphins

- Exorphins are small protein peptides that have actions like morphine but come from outside the body
- Gluten, casein and other foods can produce exorphins in susceptible individuals
- Some research has indicated that exorphins are the cause of side effects from food allergies while also stimulating cravings for the allergenic food
- Mercer ME, Holder MD. Food cravings, endogenous opioid peptides, and food intake: A review. *Appetite* 1997;29:325-52.

# Traditional Treatment Plan

- Anti-cancer medications such as methotrexate and TNF alpha inhibitors such as Remicade, Humira and Enbrel suppress the immune system
- Steroids cause long term adrenal suppression and worsening symptoms and dependance
- NSAIDS increase risk of OA, GI bleed, others
- ALL are symptom relief ONLY, don't address the cause of disease, and have serious side effects

# Relationship of the Systems

- The demonstration in the early 1980s of communications among the three main regulatory systems (nervous, endocrine, and immunological) in vertebrate organisms led to the realization that chemical signals or mediators originating from any one of these systems may influence the other two
- Haddad, J., Saade, N., and Safieh-Garabedian, B., Cytokines and neuro-immune-endocrine interactions: a role for the hypothalamic-pituitary-adrenal revolving axis, *J. Neuroimmunol.*, 133, 1, 2002.



# Communication among Systems

- Communication among and reciprocal regulation of the nervous, endocrine, and immune systems are essential for the stability of an organism. Among others, cytokines, hormones, and neuropeptides have been identified as signaling molecules mediating communications among the three systems. Neuropeptides, [active in all three systems], exhibit a number of immunomodulatory properties
- Stefano and Salzet 1999; Salzet, Vieau et al. 2000; Blalock 2005; Elmquist et al. 1997.

# LDN Mechanism of Action

Opioid Receptor Blockade for few hours while you sleep

Your body increases opioid receptors and their sensitivity

Increased endorphin production through up regulation

# Broad Effects of LDN

- → Increases enkephalin / endorphin production
- → blocks release of proinflammatory cytokines throughout the body and the gut
- → Modulates T and B lymphocyte production
- → Shift of immune response from TH2 to TH1
- → Modulates the HPG and HPA axis (Hypothalamus-Pituitary-Gonadal/Adrenal)

# Effects of LDN on Cells of the Immune System

- → Inhibits macrophage induced tumor necrosis factor (TNF) generation
- → Modulates neutrophil phagocytic activity
- → Modulates eosinophil production and actions

# How Endorphins Work

- Decrease inflammatory cytokines
- Downregulate chronic inflammatory and deigratory cells (TH2)
- Upregulate healing, regrowth, repair cells (TH1)
- Stimulate NK cell activity

# Dosing for Children or

## Highly Sensitive Adults

- Adults: start at 0.5-1.5 mg and increase by 1 pill every 2 weeks until therapeutic dosage reached, 1.5-4.5 mg or tolerable dosage.
- Liquid 1 mg/mL, start at 0.1 mL and work up slowly, increasing by 0.1 mL every 3-7 days.
- Estimate about 1 mg per 20 lbs of body weight for children. If the child is 90 lbs, give adult dosing.

# Just a note

- Research published in 2000 showed that ‘ultra low dose naltrexone’, when taken with opioid drugs, improved the efficacy of the drugs and decreased the dependence on and tolerance to the drugs. Pain. 2000 Feb;84(2-3):121-31.
- In my office, I sometimes use LDN in patients who are on low dose opioids, although I don’t let them take the two together.
- I monitor closely for side effects but have seen none.

# Take Home Message

- Second graders and endorphins are the key to how LDN works
- If you think of it, give it a try.
- LDN has such varied positive effects that it can have positive benefit in multiple disease processes: cancer, autoimmune disease, allergies, asthma, hormone balance, chronic fatigue, chronic pain, depression(?).
- When in doubt, follow the wise old adage: Start low and go slow.



Let's Talk About  
Patients and Case  
Histories Later

# Patient Stories

# Juvenile Rheumatoid Arthritis

- 13 year old female recently diagnosed with JRA
- Put on prednisone to decrease inflammation, but parents have refused immunomodulating drugs
- They have come to me for help with more natural management of JRA

# JRA, cont

- Treatment plan:
  - Gluten free diet, organic, whole food diet; supplements; better sleep habits
- LDN started at 1 mg and increased to 3 mg after 2 weeks

# JRA, cont

- After 2 weeks her symptoms were so much improved that we were able to taper her off of prednisone
- She has only had flares of pain when she eats poorly or doesn't get enough sleep
- After 1 year, her pediatrician agreed to manage her prescription and she was lost to follow up but had been doing remarkably well.

# Ulcerative Colitis

- 8 yo girl with abdominal pain, chronic bloody diarrhea and recurrent fevers, 22 lbs
- She had recurrent elevation of WBC, chronically elevated CRP and ESR
- Her doctors had tried multiple medications but couldn't get her symptoms stabilized
- Repeat colonoscopies showed worsening disease and her doctors were discussing colectomy

# UC, stabilized

- Treatment plan: dietary changes, supplements, reflexology, LDN
- LDN was started at 0.5mg and increased by 0.5 every two weeks until she got to 1.5
- 7 years later, she is still stable and symptom-free and has all her pieces with her

# Asthma & Allergies

- 9 year old boy with severe asthma requiring rescue inhaler 1-4 times daily despite daily oral and inhaled meds
- He had multiple URI requiring Abx and prednisone
- Parents had already made all household changes, used air purifiers, removed dairy, and started supplements



# Allergies & Asthma, cont

- Tx plan: supplement adjustment, yeast treatment, food sensitivity testing with resultant dietary changes
- Taught breathing techniques, breath holding
- LDN started at 0.5 mg liquid and tapered up by 0.5 mg every other week

# Asthma and Allergies, last

- Within a month he was already using less of his rescue inhalers and was having some days without use
- Within three months he was completely tapered off prednisone and all but one daily inhaler
- He has now been 3 years without an ER visit or more than rare use of rescue inhalers and no more than one URI a year

# Multiple Sclerosis

- 46 year old female, executive with demanding job who wants to return to full work but has difficulty with brain fog, severe fatigue and debilitatingly frequent exacerbations. Also poor sleep quality.
- She had already cleaned up her diet, was taking supplements, had been tested for heavy metal toxicity and treated

# MS, cont

- Treatment Plan:
  - LDN started at 1.5 mg and tapered to 4.5
  - Started on rhythmic bio-identical progesterone and estriol 8 mg
  - Cortef for adrenal support

# MS, response

- She began sleeping better within 2 weeks
- Energy levels improved and brain fog started to clear within a month
- Exacerbations became less frequent and stopped
- She has now been back at work for 5 years without an exacerbation

# Environmental Allergies

- 67 year old female with severe allergies. She'd been waking with post-nasal drip, sore throat for 30 years.
- She had Multiple sinus infections annually and chronic headaches
- Started on LDN at 4.5 mg

# Allergies, cont

- Next day came to my office and said that for the first time in over 30 years she'd woken without a sore throat or voice changes and that she felt better than she'd felt in years.
- 7 years later, she still has no problems with allergies and has only had 2 sinus infections.

# Rheumatoid Arthritis

- 63 year old female, very active, otherwise healthy woman, business owner, having difficulty maintaining her business due to fatigue and severe joint pain with deformity of her hands and elbows.
- Worsening on Methotrexate and Prednisone so her Rheumatologist recommended a second immunomodulating drug.
- That's when she came to me



# RA, Cont

- Treatment plan: dietary changes, supplements, acupuncture, microcurrent therapy, toxicity testing and treatment,
- Bio-identical hormones, adrenal support and thyroid started
- LDN started at 4.5 mg

# RA, cont

- She was tapered off all her drugs over a three week period
- 7 years later, still not on any other drugs, RA improved and has not advanced, she has no pain

# Eosinophilic Esophagitis

- 32 year old female
- Unable to eat solid food, dozens of food sensitivities, chronic throat pain, underweight
- She'd tried multiple medications without success
- She'd also tried multitudes of supplements

# Eosinophilic Esoph, Cont

- Treatment plan:
  - Diet: Eventually did a combination of food allergy elimination and macrobiotic whole foods with blood type consideration
  - Supplement, HBO, acupuncture and reflexology, frequency specific microcurrent therapy

# EE, Cont

- After 4 weeks, no improvement. She agreed to try LDN.
- Started on liquid dosing, 0.1 mg to start and an increase of 0.1 mg daily.
- When she reached 3 mg she was feeling better so she started increasing by 0.5 mg every other day.
- After 9 months at 4.5 mg, she is symptom free, eats what she wants and is chagrined to be overweight!

# Autoimmune Hepatitis

- 9 year old female with ADHD, chronic abdominal pain and headaches
- Labs showed elevated LFT, then elevated ANA
- US of liver showed biliary dilatation
- Biopsy confirmed autoimmune disease

# Autoimmune Hep, Cont

- Came to me at 11 years old on after multiple relapses and progressive disease despite medications
- Medications: recurrent prednisone and immunomodulating drugs
- Now, also fatigued, overweight, moody, poor dietary habits

# Autoimmune Hep, cont

- Treatment plan:
  - GAPS diet with food allergy testing and treatment, supplements
  - reflexology, hyperbaric oxygen, frequency specific microcurrent, neurofeedback for 3 weeks
  - LDN started at 0.5 mg and increased by 0.5 every two weeks until she reached 3.5 mg



# Autoimmune Hep, Last

- She has had fewer exacerbations, they were shorter, not as severe, responded better to therapy and became further apart
- She has had close to normal LFT's and only moderately elevated ANA on labs for 2 years.
- She is also doing well in school, is better behaved, weight is healthier
- Still taking LDN, supplements and cortef 10 mg daily

# Ulcerative Colitis

- 15 y.o. male, UC discovered incidentally after MVA
- Below average height, decreasing growth rate since he was 13, no explanation
- Felt fatigued a lot, didn't feel he was performing as well as he could in basketball
- No GI symptoms

# UC continued

- Labs? H/H 10.8/32, mild leukocytosis, Iron deficient, CRP 9.6
- Hemoccult positive, positive pANCA
- Typical lesions of mild disease on colonoscopy
- Parents refused medications

# UC continued

- Treatment plan
  - Dietary plan: gluten/casein free, organic, 'food that's just food', food allergy testing with elimination/rotation diet
  - Supplements tailored
  - LDN started at 1.5 mg and increased to 4.5 mg over 3 weeks – no problems

# UC last

- He began to respond almost immediately:
  - Anemia resolved, CRP normalized
  - Started growing again and is now taller than both parents
  - Basketball performance improved and he earned a scholarship to college
  - Grades improved
  - No lesions on follow up colonoscopy

# Hormone Imbalance

- 58 year old woman, postmenopausal, with severe, almost constant hot flashes, vaginal dryness and pain so severe that it sometimes hurt to walk, waking every 1-2 hours with night sweats, moody, fatigued
- She had osteoporosis, hypertension, dysmetabolic syndrome, chronic headaches

# Hormones, cont

- Her PCP started her on Prempro but her symptoms only worsened
- I started her on bio-identical hormones and we struggled to balance them and improve her symptoms for 2 years with no success.
- We decided to add LDN, starting at 4.5 mg (what did we have to lose?)

# LDN to the Rescue

- After starting LDN, her symptoms slowly started to improve.
- After three months, her three years of torture finally ended.
- Her hot flashes abated to once a day then once a week, her night sweats resolved, she started sleeping through the night and, best of all, the vaginal dryness was relieved and she was able to have sex again (she hugged me for that).



# Lupus

- 32 year old female with psoriasis, IBS and chronic fatigue develops joint pain, increasing abdominal pain and malar rash
- Testing confirms systemic lupus
- She refuses immunosuppressing drugs and tries to treat with supplements and healthy diet
- Contracts MRSA in hospital and worsens dramatically

# Lupus, cont

- MRSA treated with oral drugs twice, then with IV drugs when she developed sepsis. The infection keeps returning as boils.
- Antibiotics work, but she gets sicker and sicker with worsening symptoms and rising ANA although no organ damage.
- Unable to take immunomodulating drugs due to MRSA recurrence and intolerant to others for lupus, her doctors say she will die.

# Lupus, cont

- She and her husband try multiple alternative modalities, but none work.
- In my office, she receives: HBO, acupuncture, supplement tailoring, treatment for mercury toxicity, food elimination diet then rotation, treatment for yeast overgrowth; counseling recommended for the couple

# Lupus, cont

- She is started on LDN 1.5 mg, but is unable to take it due to insomnia and pruritis.
- LDN changed to liquid form and started at 0.5 mg, but she still couldn't tolerate it.
- LDN decreased to 0.1 mg and increased by 0.1 mg once a week until she reached 1.5 mg, which is where she stays.

# Lupus, resolved

- Currently still on LDN, supplements, healthy diet and lifestyle
- No recurrence of MRSA in 8 years
- No signs or symptoms of lupus and normal ANA for 7 years
- Intestinal symptoms resolved for 2 years
- Psoriasis mostly resolved
- Able to give a lecture on LDN with a clear head!

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# Autoimmune Disease NOS

- 35 year old male who, 2 years prior to presentation began having chronic fatigue, chronic body pain, moodiness to the point of disrupting his family and his job.
- After multiple doctors he was finally sent to a psychiatrist who diagnosed him with bipolar disorder and started him on medication after medication – he was on four psychotropic drugs when he presented to me.

# Autoimmune NOS, cont

- Despite all the drugs, his symptoms had continued to progress. He'd been put on disability for 'rapidly cycling bipolar disorder'.
- He continued to search for answers and finally found his way to an immunologist.
- Further testing at this time resulted in a diagnosis of 'Autoimmune Disease NOS' and 'Connective Tissue Disorder NOS'
- Diagnosis of bipolar disorder was questioned



# Autoimmune NOS, cont

- Symptoms on presentation: chronic all over body and joint pain that was so severe he sometimes could barely get out of bed; brain fog with word finding and word jumbling and extreme forgetfulness with poor concentration; markedly decreased cognitive capabilities; sensitivity to environmental stimuli; marked sensitivity to foods that changed over time; muscle spasms throughout his body; insomnia with waking every 30 minutes;

# Autoimmune NOS, cont

- In conjunction with a psychiatrist, who agreed he probably never had bipolar disorder, he was tapered slowly off his psychotropic meds.
- One of his psychiatric medications was Xanax, and this one couldn't be tapered. Every time we decreased his dosage, he had severe symptom flares.
- Testing eventually showed deficiencies in several of the liver detoxification pathways and MTHFR homozygous deficiency.

# Autoimmune NOS, cont

- He was changed to Klonopin since it can be dosed in smaller increments and tapered down 0.1 mg (compounded) monthly, which was all he could tolerate.
- All other medicines were tapered and stopped and his psychiatric symptoms stabilized
- Supplements started
- LDN started but unable to tolerate even 0.5 mg

# Autoimmune NOS, cont

- He became sensitive to all the supplements, even vitamin D, C, B causing a flare of his symptoms.
- LDN couldn't be started while Klonopin was tapered off, which took almost six months.
- After Klonopin taper, he was restarted on liquid LDN, 0.1 mg, increasing by 0.1 every 2-4 weeks.

# Autoimmune NOS, cont

- He eventually built up to only 0.5 mg, taking several months to do so.
- His sleep improved to waking only every 2 hours and he was able to add more foods without having reactions.
- His pain decreased to the point of being functional.
- His brain began to clear

# Autoimmune NOS, cont

- After 3 months at 0.5 mg, he tried again to increase and was able to get up to 1.5 mg over a period of 3-4 months.
- At 1.5 mg, he began to heal and sleep for 6 hrs.
- Four years later, he still has not been able to return to work, but he is able to care for his kids, is functional around the house and eating a healthy diet without exacerbation of symptoms. Still unable to take supplements.

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