Can LCHF and ketogenic diets improve chronic pain?

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Who we are:

Dr. Evelyne Bourdua-Roy,
LCHF/Keto/IF since 2016
Founder of Clinic Reversa

Dr. Hala Lahlou, LCHF/Keto/IF since 2016, palliative care and chronic pain management, involved in medical teaching

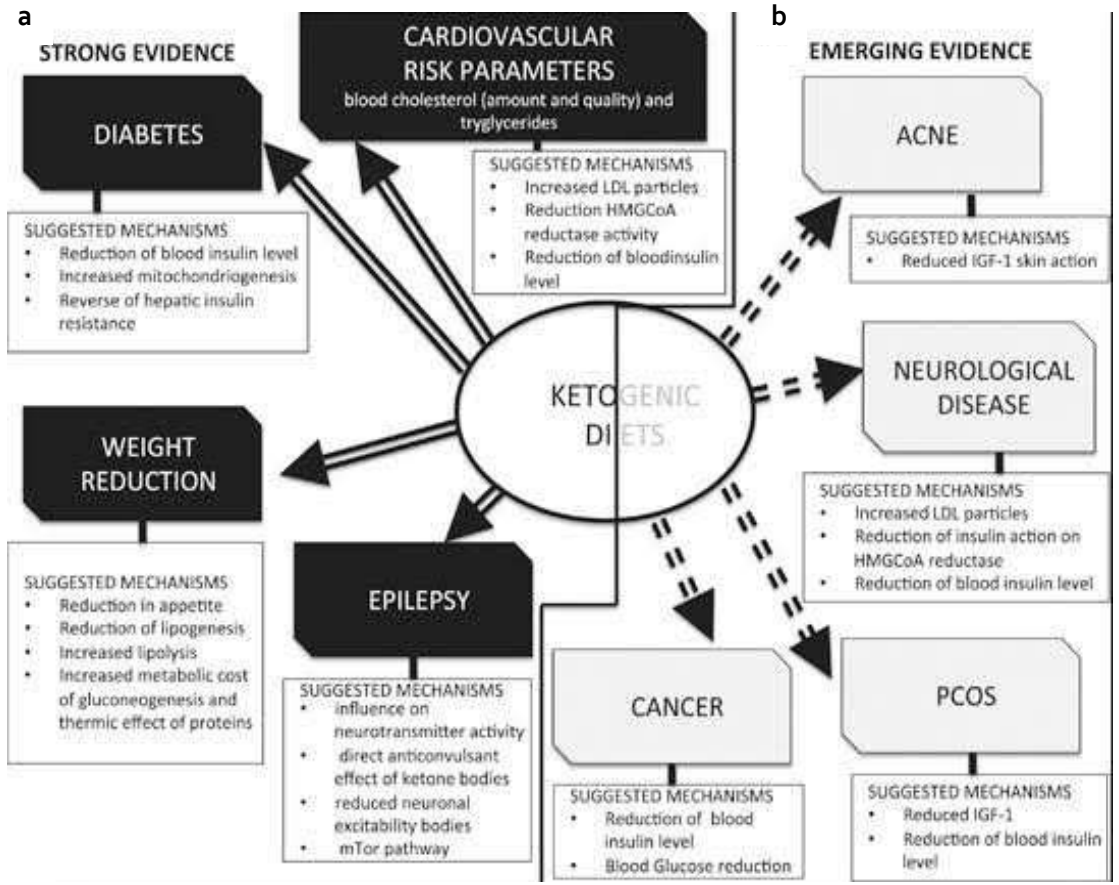
Family Physicians

Primary care clinicians

We're **not** experts in pain

No conflict of interest

Introduction



Chronic pain?

Objectives

- **Describe our clinical experience of chronic pain improvement through LCHF/keto**
- Present clinical cases of patients who experienced a significant reduction in their chronic pain
- Explore the potential **physiological and molecular mechanisms**
- Briefly mention some of the **supplements** have been associated with pain reduction

Clinical cases

56, **ankylosing spondylitis**
ImMod, NSAIDs
Constant pain, low QofL

LCHF:
- Lost 25 lbs
- NO MORE PAIN

61, **back and knee pain/osteoarthritis,**
Tylenol, sedentary due to pain

LCHF:
- Lost 20 lbs
- QofL significantly improved, PAIN ↓

Personal experience

- Chronic pain
- Impact on mood and overall functioning
- Central obesity or visceral/intraabdominal fat
- A great response to the LCHF/keto diet for pain and other related symptoms

Clinicians?

52, **fibromyalgia and IBS**
Multiple Rx, about to stop working due to pain

LCHF:
- Lost 17 lbs
- ↑ Energy, NO MORE PAIN,

43, **diabetic neuropathy and carpal tunnel syndrome, high CRP, depression**

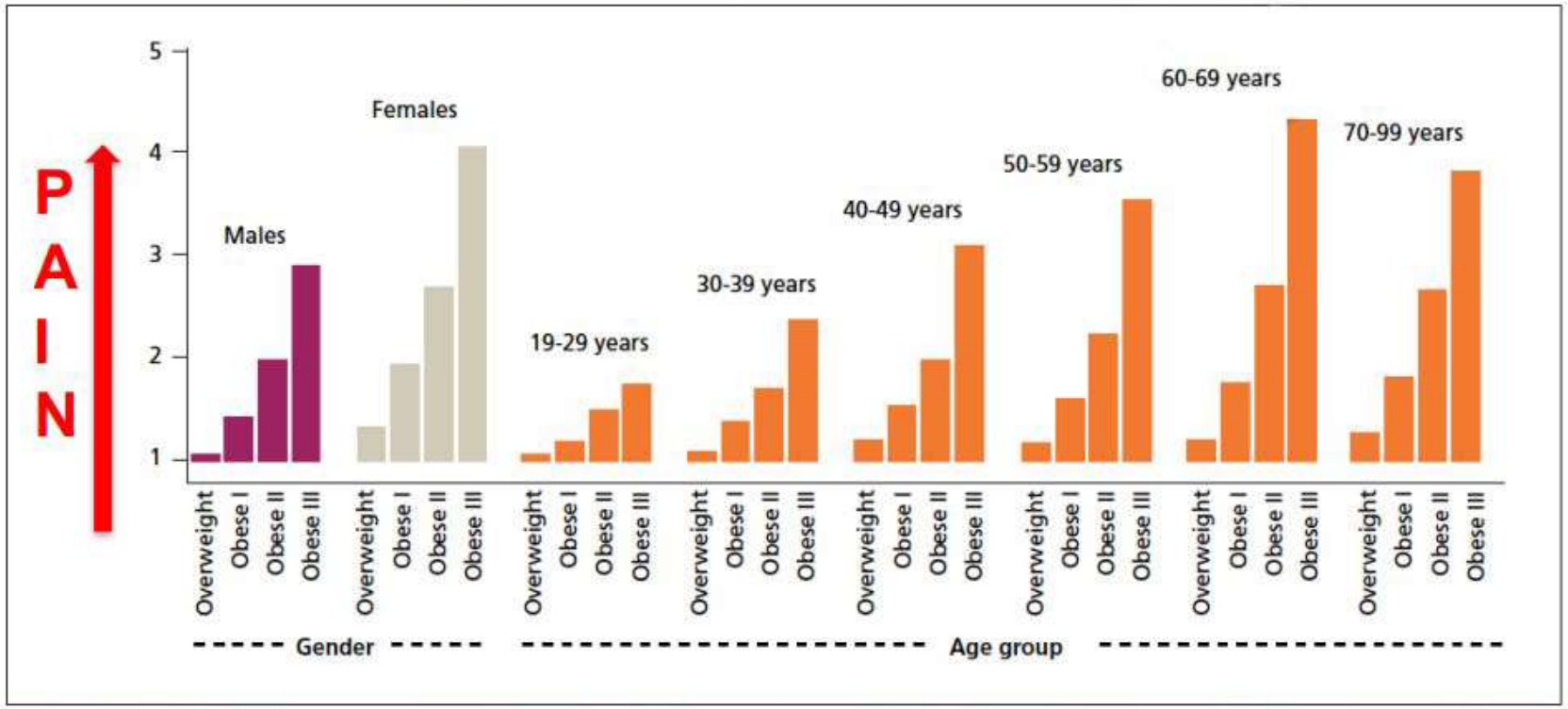
LCHF:
- Lost 12 lbs
- Improvement in mood, energy, normalised CRP
- CTS completely resolved, neuropathy ↓

What is chronic pain?

Obesity and Pain Are Associated in the United States

Arthur A. Stone and Joan E. Broderick

FIGURE 1: Odds ratios for "pain yesterday" for BMI classifications* by gender and age group[†6]



Major impacts

Impacts: Significant personal, social, and financial burden

Costs:

About 50 million Americans, costing up to $635 billions yearly (2012) → more than the yearly costs of cancer, diabetes and heart disease

How is chronic pain treated ?

Goal of treatment in chronic pain: To improve pain control, overall function and quality of life

Pharmacological approaches	Non pharmacological approaches
Chronic inflammatory disorders: - anti-inflammatories (NSAIDs, Steroids, oral vs injectable) - Disease modifying anti-rheumatic drugs (DMARDs) - Immunomodulator	Physical therapy (including TENS) Occupational therapy Massage therapy Psychotherapy
Non-inflammatory d (neuropathic, and myo - Antidepressants - Anticonvulsivants - Topical anesthetics - Nerve blocs and Plexus blocks - Intrathecal anesthetics	apies: Neuro-biofeedback Hypnosis Reiki Tai chi
Opioids (are falling out of favor for chronic pain)	Surgery (joint replacement, spinal fusion)

Diet??

The possible mechanisms through which LCHF/Keto and can improve chronic pain

- Mechanical advantages
- Anti-inflammatory pathways
- Effects of ketones bodies
- Effects on mitochondrial function
- Improved micro-nutrient status

Could chronic pain be reduced on LCHF/Keto simply because of weight loss?

- **Weight loss** with any diet can improve pain:
  - Decreased load on weight-bearing joints (hips, knees, ankles)
  - Decreased lumbar lordosis with loss of abdominal girth (chronic back pain)
  - Fat loss and decreased edema help decompress nerves such as in CTS

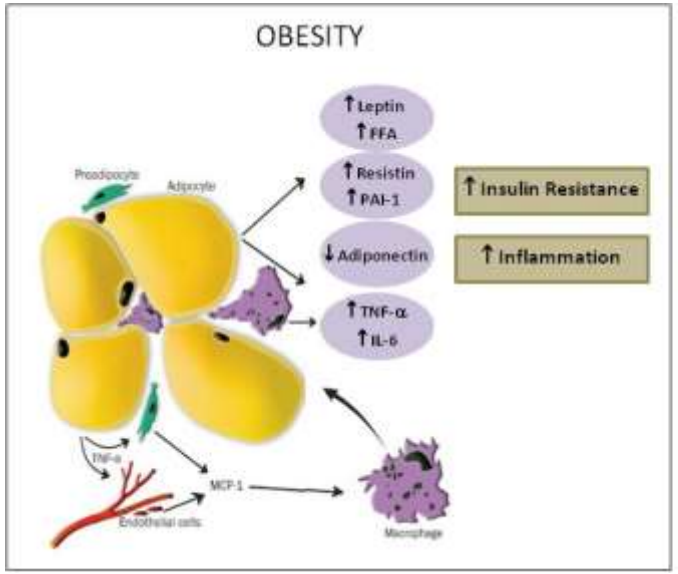
- **Weight loss** does not fully explain pain improvement because:
  - Pain decreases even before significant weight loss is achieved
  - Pain improves in non-weight bearing joints as well

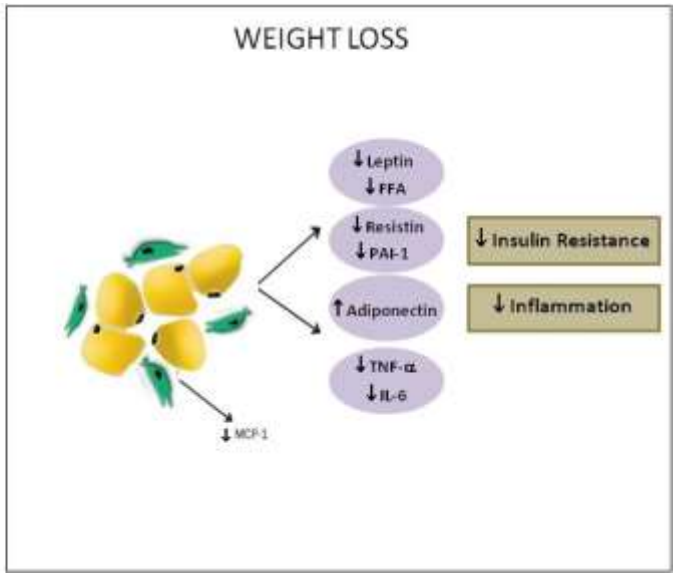
Chronic pain and chronic widespread inflammation

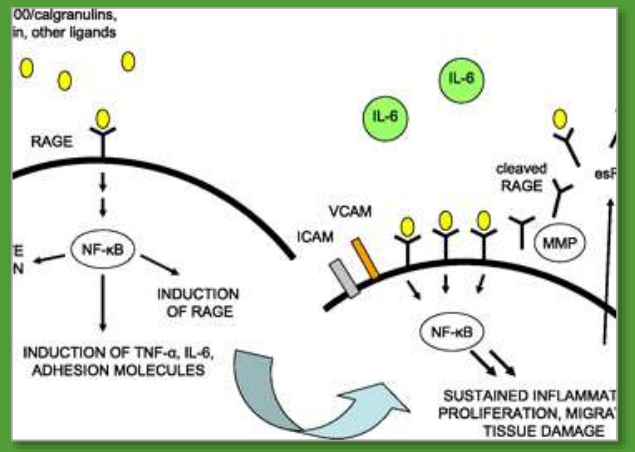
The diet-inflammation link

Many potential reasons for inflammation on a SAD:

- High circulating levels of insulin
- Central obesity and adipokines + cytokines
- Advanced end Glycation products (AGE)*
- Gut dysbiosis*
- A high Omega6 to Omega 3 fatty acid ratio*
- Post-prandial sugar spikes*





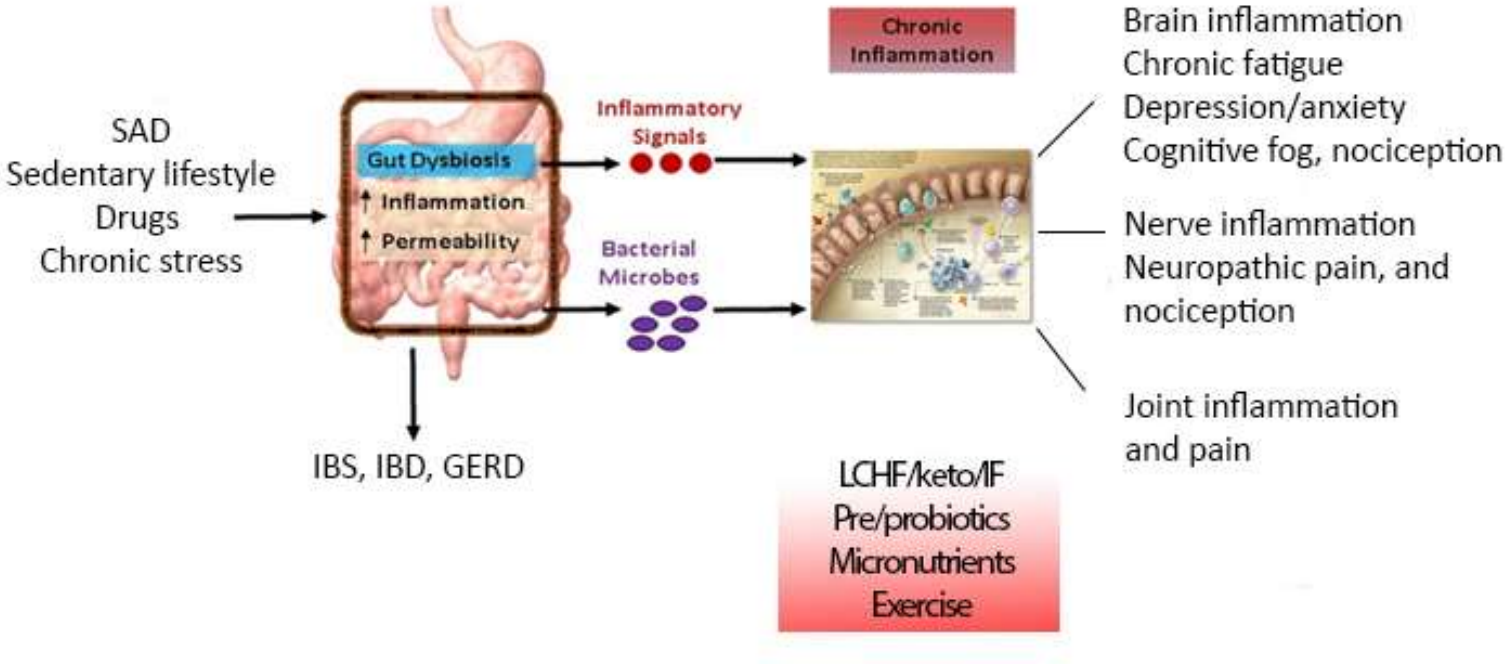


How do AGE cause inflammation and how can LCHF/Keto help?

- **Advanced glycation end-products** are either extrinsic (from food) or intrinsic (Maillard reaction inside the body)
- **AGEs bind to R-AGE**, and induce inflammatory cascades and apoptosis → tissue damage and premature aging.
- **AGEs** and chronic pain syndromes:
  - Nerve damage → neuropathic pain
  - Vascular inflammation and sclerosis → ischemic pain
  - Muscles damage → myo-fascial pain syndromes/fibromyalgia
  - Cartilage → premature aging, joint inflammation and pain/osteoarthritis
- **Anti-bodies** against AGE-receptors → decrease pain in diabetic neuropathy rat models
- **LCHF/Keto diets decrease extrinsic and intrinsic AGEs**
- **AGEs** get cleared → inflammation down-regulates and pain improves

The Journals of Gerontology: Series A, Volume 65A, Issue 9, 1 September 2010, Pages 963–975

Gut dysbiosis, inflammation, and the role of LCHF/Keto



***Caveat:**

Lectin laden foods, some FODMAPs, and dairy may still cause inflammation and local symptoms in susceptible individuals.

Microbiome. 2017; 5: 80.

Omega 6:3 ratio, inflammation and the positive effects of an LCHF/Keto diet

Omega-6 fatty acids can be converted through different pathways to inflammatory or anti-inflammatory molecules

Omega-3 fatty acids are known to reduce inflammation

- SAD = 10:1 up to 25:1
- 4:1 for healthy individuals
- 1:1 preferred in inflammatory conditions for treatment

(Covington M. Am Fam Phys. 2004;70:133-140)

LCHF and Keto diets recommend

+ Reduced intake of omega-6 rich vegetable oils, by replacing them with fruit oils.

+ Increased intake of omega 3 rich foods

→ Better ratio!

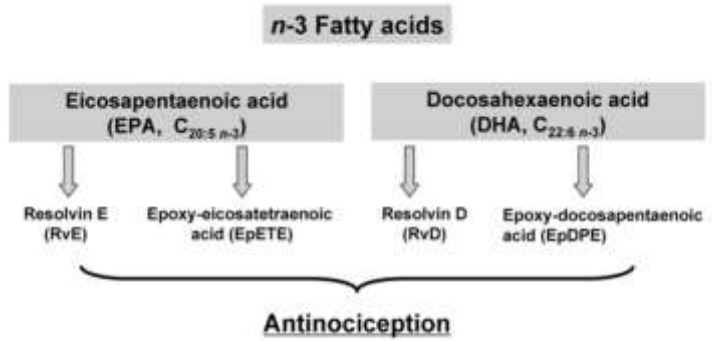


Fig. 6. Metabolites Derived from *n*-3 Polyunsaturated Fatty Acids and Their Association with Pain

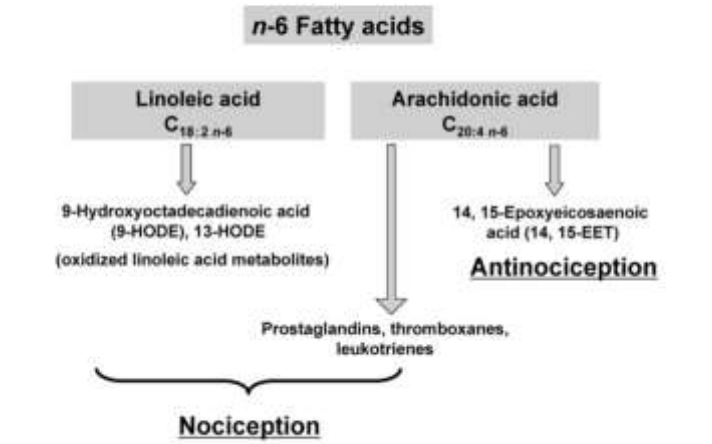
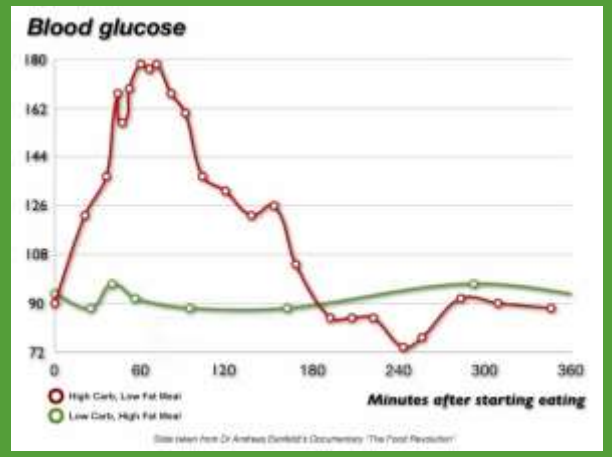


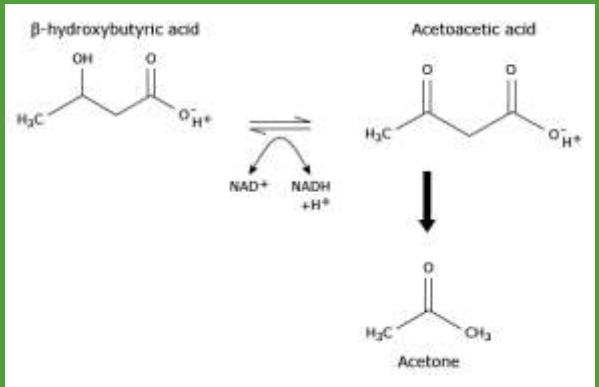
Fig. 7. Metabolites Derived from *n*-6 Polyunsaturated Fatty Acids and Their Association with Pain



Post prandial sugar spike and inflammation

- Low insulin diet may decrease plasma C- reactive protein, and tended to increase serum adiponectin concentrations
  (McCarty MF Low-insulin-response diets may decrease plasma C- reactive protein by influencing adipocyte function Medical Hypotheses 2005 64(2):385-7) and (Neuhouser ML, Schwarz Y, Wang C, et al. A Low-Glycemic Load Diet Reduces Serum C-Reactive Protein and Modestly Increases Adiponectin in Overweight and Obese Adults. The Journal of Nutrition. 2012;142(2):369-374. doi:10.3945/jn.111.149807.)
- High glycemic load correlates positively with plasma CRP
  (Liu S. Manson JE. Buring JE. Stampfer MJ. Willett WC. Ridker PM.)
- Relation between a diet with a high glycemic load and plasma concentrations of high-sensitivity C- reactive protein in middle-aged women (American Journal of Clinical Nutrition 2002 75(3):492-8)

Are ketones beneficial for pain control?



Could the benefits also be due to ketone bodies?

Positive effects even in the absence of ketosis in LCHF

We have numerous patients with significant pain improvement who are not in ketosis

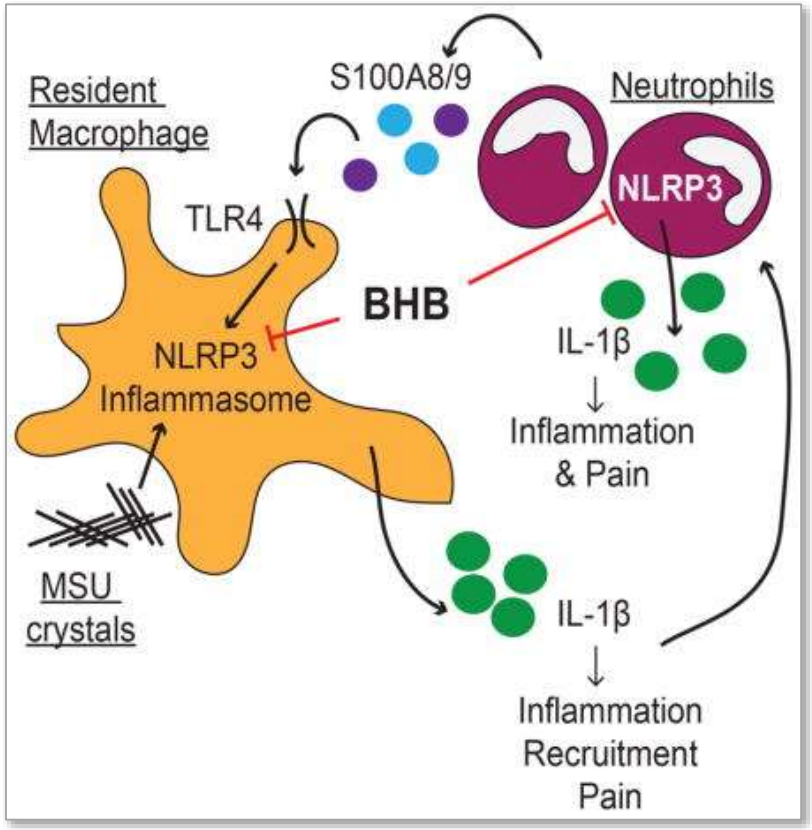
Ketone bodies can improve pain signaling:

- Anti-inflammatory effects
- Anticonvulsive effects
- Improve mitochondrial function and biogenesis
- Adenosine signaling

Ketone bodies can decrease inflammation

In 2015, a study by Youm, D'Agostino, et al concluded that « BHB reduces NLRP3 inflammasome-mediated interleukin (IL)-1β and IL-18 production in human monocytes. In vivo, BHB or a ketogenic diet attenuates caspase-1 activation and IL-1β secretion in mouse models of NLRP3-mediated diseases such as Muckle-Wells syndrome, familial cold autoinflammatory syndrome and urate crystal-induced peritonitis. **Our findings suggest that the anti-inflammatory effects of caloric restriction or ketogenic diets may be linked to BHB-mediated inhibition of the NLRP3 inflammasome** ».

Later in 2017, it has been demonstrated by Goldberg and his team that **BHB can also relieve the inflammatory pain of acute gout in rat models**.



Cell Rep. 2017 Feb 28;18(9):2077-2087

Nat Med. 2015 Mar;21(3):263-9

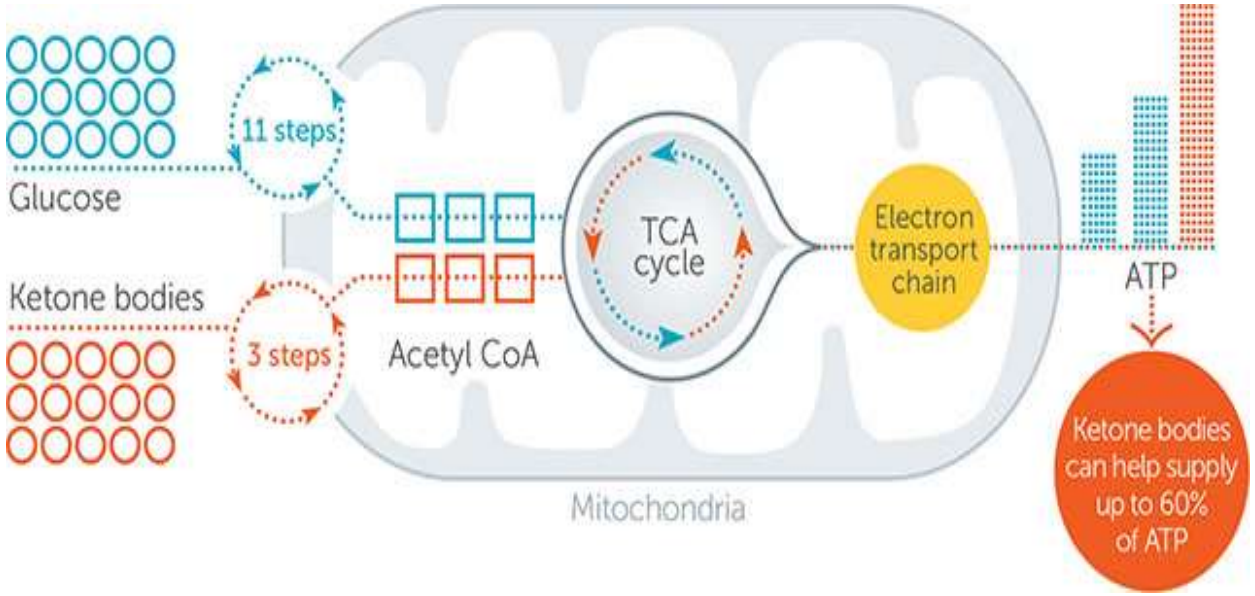
The CNS effects of ketones, and their benefits for analgesia

- **Acetone:** anticonvulsive effect (via K+ channels)
- **Acetone:** inhibition of NMDA receptors
- **Aceto-acetate:** reduces synaptic glutamate → post synaptic neuronal excitability decreases
- **Beta hydroxybutyric acid and acetone** enhance inhibitory glycine receptors and act as anesthetics
- **Beta-hydroxybutyric acid** enhances $GABA_A$ receptor function

Could it be due to improved mitochondrial function?

Mitochondria are affected in fibromyalgia and chronic fatigue syndrome:

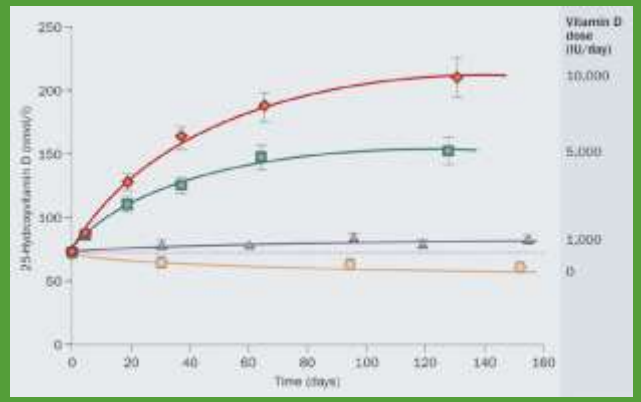
- Altered structure and function
  - Efficacy in glucose oxidation down to 70%
  - Increased production of lactic acid in muscles
- Consequence = increased oxidative stress, reactive oxygen species and upregulation of inflammatory cascades



LCHF & Keto diets, and their impact on adenosine

- Fasting, and ketogenic diets boost adenosine signaling.
- Adenosine acts like a neuromodulator.
- Adenosine not only has an anti-inflammatory effect but also modulates pain, anxiety and sleep pathways.
- Recent studies show that acupuncture and exercise benefits in the treatment of chronic pain seem to be adenosine mediated.

Is there a link between micronutrients and pain?



Vitamin D and pain.

VITAMIN D is often deficient in overweight and obese people. It is also endemic in the Western world due to reduced sun exposure.

- Important role in neuronal regulation and modulation of GABA and NMDA.
- Inflammatory pathways associated with chronic pain like TGF-beta-1, Interleukin-4 and nitric oxide (NO) are **regulated** by vitamin D.
- Vitamin D deficiency → myopathy of type II muscle fibers, bony pain, deep muscle hypersensitivity and balance deficit.

Recommended doses: 50 to 75 IU/kg/day. Each increase of 1000 IU increases average blood levels by 25 nmol/L (10 ng/ml). Maximum safe daily intake 10,000 IU. Optimal range: 125-150 nmol/L (50-60 ng/ml). Toxicity > 500 nmol/L

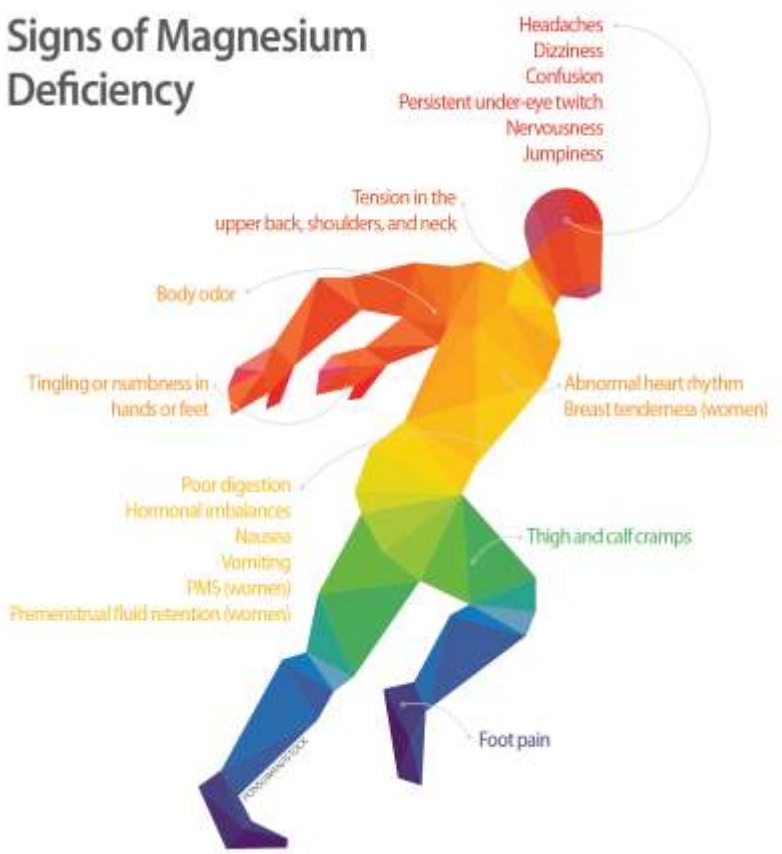
Magnesium and pain

Magnesium deficiency is also associated with pain, fatigue, and neuronal hyperexcitability, neuropathic pain

Magnesium intake is often insufficient in a SAD. 68% consume less than RDA and 19% less than half of the magnesium RDA

LCHF and keto diets by decreasing insulin secretion, cause more Mg2+ loss through the kidneys

Mg2+ supplements are of paramount relevance in this WOE, and especially in those living with chronic pain



Recommenced doses: 300-400mg/day to start, bisglycinate is the favored form for chronic pain as it is well absorbed and glycine may also help in pain signaling pathways. Migraines 600 mg/day

Other supplements that have some data supporting their use in chronic pain

- **Omega-3** in RA: up to 7.5 g/d, aim for 1:1 if active disease, maintenance: 2.5 g/d of EPA/DHA
- **Riboflavin:** 400 mg/day in migraines
- **Coq10:** 100 mg TID in migraines and fibromyalgia
- **Curcumin:** 8 RCTs → 1000 mg/day of curcumin for arthritis
- **Glucosamine sulfate:** 1500 mg/day for years
- **Probiotics:** may help, studies in RA, but types and doses unclear

- **Other nutrients linked to pain:** vitamin B1, Vitamin B2, folate, calcium, amino acids, zinc, carnitine

Food, mood, and pain ...

Could it be due to an improved psychological state?

LCHF and ketogenic diets improve:

- mood
- attention and concentration
- cognition
- energy

→Result in more motivation and sense of control

→Result in less despair and helplessness

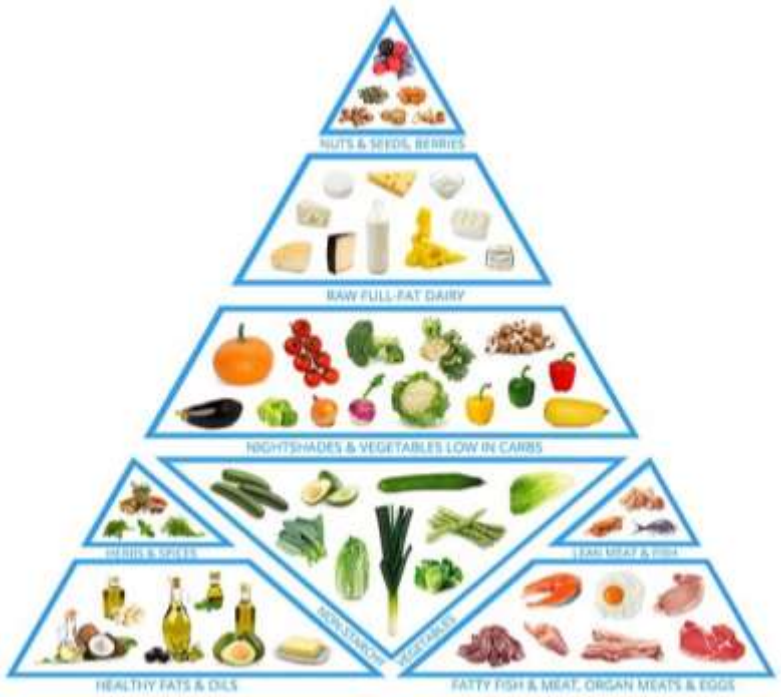
→Result in decreased pain perception and improved pain tolerance

Multifactorial improvement and positive feedback loop: decreased pain and increased quality of life

An all-in-one magic pill?

Pharmacological approaches	Nutritional approach with LCHF/keto
Chronic inflammatory disorders: - anti-inflammatories (NSAIDs, Steroids, oral vs injectable) - Disease modifying anti-rheumatic drugs (DMARDs) - Immunomodulators	Decrease of inflammation through: - Reduction of adipokines - Decrease of glycation endproducts - Improvement of microbiome - Improved omega6:3 ratio - Anti-inflammatory effects of the ketone bodies
Non-inflammatory disorders (neuropathic, and myofascial pain): - Antidepressants - Anticonvulsivants - Topical or intrathecal anesthetics - Nerve and plexus blocks - Antagonists of NMDA receptors	Analgesia through: - Antidepressamt effects of ketone bodies (?) - Anticonvulsive effects of ketone bodies - Antalgic effect of adenosin - Decreased pain associated with vitamin D and magnesium deficiency
Opioids	Improvement in energy and endurance leading to more exercise!!!!

Chronic pain? Think diet as a therapeutic option!



Although many patients are convinced of the importance of food in both causing and relieving their problems, many doctors' knowledge in nutrition is rudimentary. Most feel more comfortable with drugs than foods, and the "food as medicine" philosophy of Hippocrates has been largely neglected.

Mark Lucock, in Smith R. *Let food be your medicine…*, BMJ 2004;328, doi 10.1136/bmj.328.7433.0-g.

Thank you!

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