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The Role of Mitochondrial Function in Autoimmune Diseases

Analysis by Dr. Joseph Mercola | August 19, 2024

STORY AT-A-GLANCE

- There are more than 80 different autoimmune diseases, including Type 1 diabetes, multiple sclerosis, lupus and rheumatoid arthritis
- Research highlights the crucial role of mitochondrial function in the development and progression of autoimmune conditions
- Most people have dysfunctional mitochondria, and if you don't have enough mitochondria, you can't create cellular energy efficiently enough to ward off chronic diseases, including autoimmune diseases
- When damaged mitochondria or their components are released into a cell or the surrounding area, they can trigger inflammation because your immune system recognizes them as foreign, similar to bacteria
- Improving your mitochondrial function to increase cellular energy is key to preventing and managing autoimmune diseases

Autoimmune diseases occur when your body's immune system mistakenly attacks its own cells, tissues and organs. Normally, your immune system protects your body from potentially harmful invaders like bacteria and viruses. However, in autoimmune diseases, your immune system fails to distinguish between dangerous pathogens and your body's cells, leading to inflammation and tissue damage.

There are more than 80 different autoimmune diseases, including Type 1 diabetes, multiple sclerosis, lupus and rheumatoid arthritis.[1] Other examples include inflammatory bowel disease and psoriasis.

While it's often said the exact cause of autoimmune diseases is unknown, research highlights the crucial role of mitochondrial function in the development and progression of these conditions. Most people have dysfunctional mitochondria, and if you don't have enough mitochondria, you can't create cellular energy efficiently enough to ward off chronic diseases, including autoimmune conditions.

Autoimmune Diseases Are an Epidemic

Autoimmune diseases affect an estimated 50 million Americans, making them the third most common disease category, behind only cancer and heart disease.[2] Close to 80% of those affected are women,[3] and autoimmune diseases represent a leading cause of death among young and middle-aged women.[4]

Further, research suggests there's been a "steady rise in autoimmune disease throughout Westernized societies over the last decades."[5] Overall, it's estimated that the incidence of autoimmune diseases worldwide is increasing 19.1% yearly and, according to Dr. Frederick Miller, Ph.D., scientist emeritus with the National Institute of Environmental Health Sciences:[6]

> *"Not only are core currently recognized autoimmune diseases increasing, but the range of autoimmune and chronic inflammatory diseases continues to expand in number and scope, as additional disorders are found to have laboratory or clinical features implicating involvement of the immune system and autoimmune signatures."*

Miller cites environmental factors, including dietary changes and their effects on microbiomes, stress, air pollution and xenobiotics, such as environmental pollutants, household chemicals, food additives and pharmaceuticals, as potential contributing

factors to the rise in autoimmune diseases. Importantly, these factors can significantly affect mitochondrial function as well.

In an opinion piece in Scientific American, Miller and coauthor Olivia Casey, senior director of programs of the Autoimmune Association, describe autoimmunity as an epidemic, stating:[7]

> *"As a person's own immune system attacks their body instead of microbes or cancerous cells, they can experience chronic fatigue, chronic pain, drug dependency, depression and social isolation. These symptoms annihilate mental health, wreck promising careers, destroy lives and, often, ruin families. For too many, these illnesses result in early death.*
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> *… Most autoimmune diseases are being diagnosed in increasing numbers ranging from 3% to 12% annually across the globe. We also are finding more people with autoantibodies — immune system proteins that, instead of ignoring our cells and organs, treat them as invaders. Autoantibodies are markers for the presence, or the possible development, of autoimmune diseases.*
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> *Our recent research indicates that one type of autoantibody called antinuclear antibodies increased nearly 50% in the U.S. in less than 30 years. This is not simply because we are screening more people. Even more concerning, teenagers in the study experienced a nearly 300% increase between 1988 and 2012. Many of these children might not ever achieve their full potential, because battling chronic illness will alter their lives."*

How Mitochondrial Function Affects Autoimmune Disease

Mitochondria, often referred to as the powerhouses of the cell, play a crucial role in energy production and cellular metabolism. They're also involved in regulating immune responses, to the extent that they've been described as the "powerhouses of immunity" as well.[8]

"At the organelle level, mitochondria have emerged as critical participants in initiating and progressing multiple autoimmune diseases," researchers with the Chinese Academy of Medical Sciences explained. "And the fact that mitochondria interact with the immune system can give a reasonable explanation of how mitochondria are involved in the pathogenesis of autoimmune diseases."[9]

Malfunctioning mitochondria play a key role in immune system problems. Damaged mitochondria can't support important signaling molecules, such as mitochondrial antiviral signaling protein (MAVS), which is crucial for certain immune responses. Debris from damaged mitochondria, such as mitochondrial DNA, can also trigger abnormal inflammation.

Disrupted mitochondrial metabolism, especially the generation of reactive oxygen species (ROS), further affects the release of inflammatory molecules, antimicrobial responses and activation of immune cells. Therefore, it's essential to maintain enough healthy mitochondria to keep your immune system running optimally.[10]

A review published in Nature Reviews Rheumatology shed more light on the role of mitochondria in autoimmune diseases, explaining that when damaged mitochondria or their components are released into a cell or the surrounding area, they can trigger inflammation because your immune system recognizes them as foreign, similar to bacteria.[11]

Additionally, in autoimmune diseases, your body's antibodies can attack mitochondria, indicating "an interplay between the adaptive immune system and mitochondria," the researchers noted. This again highlights the importance of healthy mitochondria in preventing and managing autoimmune conditions.

Mitochondrial Dysfunction Linked to Lupus, Rheumatoid Arthritis and Type 1 Diabetes

Studies show mitochondrial dysfunction in various autoimmune diseases, including lupus. "Mitochondria in T cells of SLE [systemic lupus erythematosus] patients have a

high mitochondrial membrane potential and decreased ATP production, indicating mitochondrial damage," scientists with the University of Groningen in the Netherlands noted.[12]

In terms of rheumatoid arthritis (RA), they stated, "Mitochondrial DNA has also been found to be increased in the plasma of RA patients. This mitochondrial DNA may act as a DAMP [mitochondrial danger associated molecule] and induce or maintain inflammatory responses in RA … mitochondria in T cells in RA have defective DNA repair mechanisms, which is associated with low mitochondrial oxygen consumption and ATP production."[13]

Mitochondrial dysfunction, including decreased adenosine triphosphate (ATP) — the energy currency of your body — production, has also been found in connection with Type 1 diabetes. The scientists stated:[14]

> *"T cells isolated from Type 1 diabetic patients show decreased ATP production, also indicating mitochondrial dysfunction. Since this mitochondrial dysfunction was only observed in Type 1 diabetes and not in Type 2 diabetes, it is assumed that mitochondrial dysfunction in Type 1 diabetes does not result from metabolic abnormalities and that this mitochondrial dysfunction may play a role on the pathogenesis of Type 1 diabetes."*

Do Vaccines and mRNA Jabs Play a Role in Autoimmune Disease?

There are likely many environmental factors that contribute to the development of autoimmune disease. Vaccines and mRNA COVID-19 shots are among them.

Yehuda Shoenfeld, a world expert in autoimmune diseases who heads the Zabludowicz Autoimmunity Research Centre at the Sheba Hospital in Israel, used the term autoimmune syndrome induced by adjuvants (ASIA) to describe autoimmune conditions that may be triggered by exposure to a vaccine or other stimuli.

A team of researchers from Italy explained in the European Association for Predictive, Preventive and Personalized Medicine Journal:[15]

> *"Molecular mimicry and bystander activation are reported as possible mechanisms by which vaccines can cause autoimmune reactions.*
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> *The individuals who might be susceptible to develop these reactions could be especially not only those with previous post-vaccination phenomena and those with allergies but also in individuals who are prone to develop autoimmune diseases, such as those with a family history of autoimmunity or with known autoantibodies, and the genetic predisposed individuals."*

ASIA syndrome has also been reported in people who received COVID-19 shots, including female health care workers, as have cases of **vaccine-induced Graves' disease**, which developed just three days after a COVID-19 injection.

Optimizing Cellular Energy Production Is Essential for Autoimmune Disease

Optimizing your mitochondrial function is one of the most important strategies to optimize your cellular energy, so it's at the core of preventing and managing autoimmune diseases. Excess intake of linoleic acid (LA) — found in the seed oils used in most ultraprocessed foods.

Estrogen dominance, I believe, is another leading contributor to mitochondrial dysfunction, and I believe is the primary reason why most autoimmune diseases are, like rheumatoid arthritis and multiple sclerosis, are much higher in women. Seed oils and estrogen both:

- Increase free radicals that cause oxidative stress and damage your mitochondria's ability to produce energy
- Increase calcium inside the cell that causes an increase in nitric oxide and superoxide that increases peroxynitrite that also increases oxidative stress

- Cause an increase in intracellular water causing your body to retain water
- Slow down your metabolic rate and suppress your thyroid gland

How to Use Progesterone

Before you consider using progesterone it is important to understand that it is not a magic bullet, and that you get the most benefit by implementing a Bioenergetic diet approach that allows you to effectively burn glucose as your primary fuel without backing up electrons in your mitochondria that reduces your energy production. My new book, "Your Guide to Cellular Health: Unlocking the Science of Longevity and Joy," covers this process in great detail.

Once you have dialed in your diet, an effective strategy that can help counteract estrogen excess is to take transmucosal progesterone (i.e., applied to your gums, not oral or transdermal), which is a natural estrogen antagonist. Progesterone is one of only three hormones I believe many adults can benefit from. (The other two are DHEA and pregnenolone.)

I do not recommend transdermal progesterone, as your skin expresses high levels of 5-alpha reductase enzyme, which causes a significant portion of the progesterone you're taking to be irreversibly converted primarily into allopregnanolone and cannot be converted back into progesterone.

Ideal Way to Administer Progesterone

Please note that when progesterone is used transmucosally on your gums as I advise, the FDA believes that somehow converts it into a drug and prohibits any company from advising that on its label. This is why companies promote their progesterone products as "topical."

However, please understand that it is perfectly legal for any physician to recommend an off-label indication for a drug to their patient. In this case progesterone is a natural

hormone and not a drug and is very safe even in high doses. This is unlike synthetic progesterone called progestins that are used by drug companies, but frequently, and incorrectly, referred.

Dr. Ray Peat has done the seminal work in progesterone and probably was the world's greatest expert on progesterone. He wrote his Ph.D. on estrogen in 1982 and spent most of his professional career documenting the need to counteract the dangers of excess estrogen with low LA diets and transmucosal progesterone supplementation.

He determined that most solvents do not dissolve progesterone well and discovered that vitamin E is the best solvent to optimally provide progesterone in your tissue. Vitamin E also protects you against damage from LA. You just need to be very careful about which vitamin E you use as most supplemental vitamin E on the market is worse than worthless and will cause you harm not benefit.

It is imperative to avoid using any synthetic vitamin E (alpha tocopherol acetate — the acetate indicates that it's synthetic). Natural vitamin E will be labeled "d alpha tocopherol." This is the pure D isomer, which is what your body can use. There are also other vitamin E isomers, and you want the complete spectrum of tocopherols and tocotrienols, specifically the beta, gamma, and delta types, in the effective D isomer.

There are also other vitamin E isomers, and you want the complete spectrum of tocopherols and tocotrienols, specifically the beta, gamma, and delta types, in the effective D isomer. As an example of an ideal vitamin E you can look at the label on our vitamin E in our store. You can use any brand that has a similar label.

You can purchase pharmaceutical grade bioidentical progesterone as Progesterone Powder, Bioidentical Micronized Powder, 10 Grams for about $40 on many online stores like Amazon. That is nearly a year's supply, depending on the dose you choose.

However, you will need to purchase some small stainless steel measuring spoons as you will need a 1/64 tsp which is 25 mg and a 1/32 tsp which is 50 mg. A normal dose is typically 25 to 50 mg and is taken 30 minutes before bed, as it has an anti-cortisol function and will increase GABA levels for a good night's sleep.

If you are a menstruating woman, you should take the progesterone during the luteal phase or the last half of your cycle, which can be determined by starting 10 days after the first day of your period and stopping the progesterone when your period starts.

If you are a male or non-menstruating woman you can take the progesterone every day for four to six months and then cycle off for one week. The best time of day to take progesterone is 30 minutes before bed as it has an anti-cortisol function and will increase GABA levels for a good night's sleep.

This is what I have personally doing for over a year with very good results. I am a physician so do not have any problems doing this. If you aren't a physician you should consult one before using this therapy, as transmucosal progesterone therapy requires a doctor's prescription.

The Gut Microbiome: A Delicate Balance for Optimal Health

Your gut microbiome is a complex ecosystem where trillions of bacteria coexist in a delicate balance crucial for your overall health. At the heart of this system are oxygen-intolerant bacteria, which play a vital role in converting indigestible plant fibers into beneficial fats like butyrate and propionate.

These bacteria thrive on both soluble and insoluble plant fibers, creating a beneficial cycle of growth and decay within the colon. On the other hand, a key characteristic of oxygen tolerant (pathogenic) bacteria is the presence of endotoxin in their cell walls, which has significant implications for human health.

Dr. Ray Peat's pioneering work in bioenergetics emphasized the importance of maximizing cellular energy production for optimal health. This concept, not yet fully appreciated by many healthcare professionals, suggests that insufficient cellular energy production is at the root of most diseases.

A critical factor in maintaining a healthy gut microbiome is the ability to maintain an oxygen gradient in the large intestine. This gradient creates an ideal environment for oxygen-intolerant bacteria. However, this process requires adequate cellular energy.

When energy is lacking, the body struggles to maintain this gradient, leading to shifts in bacterial populations.

While Peat's work was groundbreaking, it may not have fully accounted for the varying toxicities of endotoxins produced by different types of bacteria. Some individuals experience benefits from avoiding plant carbohydrates, which reduces endotoxin production. However, the situation is more complex than initially thought.

The widespread use of seed oils and exposure to other toxins has compromised many people's ability to produce sufficient mitochondrial energy. This energy deficiency limits the body's capacity to effectively remove oxygen from the large intestine, causing a shift from predominantly oxygen-intolerant bacteria to oxygen-tolerant species.

As a result, individuals with gut microbiomes dominated by oxygen-tolerant bacteria may experience more severe reactions to plant carbohydrates due to the increased endotoxin load.

Understanding the intricate relationship between cellular energy production, oxygen gradients, and the gut microbiome is crucial for achieving optimal health. By supporting mitochondrial function and maintaining a balanced gut environment, you can promote the growth of beneficial oxygen-intolerant bacteria and minimize the impact of harmful endotoxins.

When the balance of gut bacteria is disrupted and oxygen-intolerant bacteria populations decrease, leaky gut can develop. This condition compromises the intestinal lining, allowing toxins, undigested food particles, and harmful microbes to enter the bloodstream. The resulting systemic inflammation can lead to various chronic health issues.

In a healthy gut, oxygen-intolerant bacteria produce short-chain fatty acids (SCFAs), particularly butyrate, which nourish colon epithelial cells and strengthen the gut barrier. These SCFAs also stimulate goblet cells to produce mucin, a key component of the protective mucus layer in the colon. This mucus shield defends against pathogenic bacteria and abrasive forces that could compromise gut integrity.

By nurturing beneficial oxygen-intolerant bacteria, you can fortify your gut barrier, reduce the threat of harmful endotoxins, and cultivate a thriving internal ecosystem that supports your overall well-being.

What You Can Do Now

Next month I hope to publish my new book Cellular Health, The Unified Theory of All Disease for Ultimate Longevity and Joy. Till then you can implement the following to reap the benefits.

- Lower your LA intake as low as possible by avoiding processed foods, seed oils, chicken, pork, seeds and nuts and review my classic **article on LA**.
- Take progesterone, mixed with natural vitamin E, as described above.
- Make sure you're eating healthy carbs such as ripe fruit, raw honey and maple syrup. My new book identifies 12 different classification of carbs so you can use the ones that are just right for your current state of health.
- Reduce your stress, as chronic stress promotes cortisol release, which is a potent suppressor of mitochondrial function and biogenesis. **Progesterone** can be quite helpful here, as it's a potent cortisol blocker.
- Take supplemental **niacinamide**, as your mitochondria cannot make energy without it. I recommend taking 50 mg of niacinamide three times a day.

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