WHY WE NEED A HIGH LYSINE DIET

PART 1

Do you suffer from shingles or cold sores? Do you have joint pain? Have you tried going gluten-free but still get bloated? Do you suffer from Candida, inflammation, colds, or allergies? Are you low in calcium and iron? Do you have high blood pressure, high blood sugar, or hair loss? Do you have anxiety, depression, or low energy? Are you inattentive, or have poor short-term memory? A diet that is low in the amino acid lysine and high in arginine can lead to all these problems, and much more. Lysine is an essential amino acid, so it must be obtained in our diet, but the body makes all the arginine it needs. Dietary arginine competes with lysine for absorption; thus, it interferes with actions of lysine. In addition, the effects from excess arginine lead to many health problems.

BENEFITS OF A HIGH LYSINE/LOW ARGININE DIET

Lysine is so fundamental to health that the benefits of a high lysine/low arginine diet are considerable! Lysine is needed for: calcium absorption, collagen, healthy sexual development and fertility, growth and development, antioxidants, methylation and detoxification, healthy weight and energy production, healthy heart and kidneys, mental and neurological health, a strong, functional immune system, pain relief, a healthy pancreas, and cancer prevention. Lysine is one of only two amino acids that's broken down only into ketones, rather than glucose, which provide energy for the heart. Many amino acids are made in the body out of other amino acids, but we must get our lysine from our diet, so it's an essential amino acid.

In contrast, we make all the arginine we need, as a study showed, except in certain cases, and the effects of excessive arginine include providing a "terrain" that supports pathogens, as well as cancer. In an inflammatory situation, excessive arginine increases inflammatory nitric oxide with its very harmful free radical peroxynitrite (including in the brain), which causes kidney damage, high homocysteine, low glutathione, and even death. In addition, arginine becomes glucose rather than ketones, it raises insulin (which signals for fat storage), and decreases satiety, thus **increasing meal frequency** more than other amino acids.

Just a few health problems related to lysine deficiency include kidney stone formation, low thyroid hormone production, asthma, chronic viral infections, and abnormal growth and development, and a deficiency can cause nausea, fatigue, dizziness, anemia, and loss of appetite. Some disorders of the reproductive system have also been linked to a lack of lysine in the diet.

MY VEGETARIAN DIET

As a vegetarian for 35 years, I assumed I had a healthy diet. My peanut butter was organically grown, I sprouted my almonds, soaked my oatmeal, and ate only whole grain sprouted bread, and I cooked my chickpeas for hours to make hummus. I also faithfully followed the

recommendation to have 1 to 2 ounces of 80% cacao per day, carrying a large bar in my purse. But I seemed to have no energy, had bad dental health, was depressed, and had trouble sleeping. I was going through a stressful time, which certainly contributed, but stress can't be avoided. Then I got a number of compression fractures in my spine while doing just normal movements, and was diagnosed with adrenal fatigue and osteoporosis. I even fainted twice, often woke up with a rapid heartbeat, and finally had hip, back, shoulder and neck pain to the point of being disabled. In short, I felt like I was literally falling apart.

Although I was a staunch vegetarian, I added fish to my diet, but there didn't seem to be any improvement. So, I looked into ways to increase calcium for the osteoporosis. Calcium is needed for tooth enameling too, so I figured that more calcium would help with my dental health. I learned that lysine increases calcium absorption and decreases calcium loss in urine, so it might help prevent and treat osteoporosis. Dietary L-lysine and calcium metabolism in humans - PubMed (nih.gov) In addition, it helps with problems of excessive calcification, like torn rotator cuff, Rotator cuff calcific tendinopathy: from diagnosis to treatment - PMC (nih.gov) calcified arteries (coronary artery disease), Shimomura, A, et al, Dietary L-lysine prevents arterial calcification in adenine-induced uremic rats. J Am Soc Nephrology 25(9) 1954-65 (March 20, 2014), and kidney calcium-oxalate stones and oxalate crystals. This is because lysine dissolves oxalate crystals and prevents their formation-by controlling calcium absorption. Influence of the lysine on the calcium oxalate renal calculi | Request PDF (researchgate.net) Oxalate crystals in muscles and joints cause pain, and I had been eating a lot of the foods that are highest in oxalates: spinach, almonds, and sweet potatoes, also green tea. Ouch! Oxalates and Pain - INTEGRATIVE PAIN SCIENCE INSTITUTE

One way lysine regulates calcium is through the cholesterol transporter NPC-1, which also is needed for autophagy. Autophagy clears away damaged cells to be replaced with new cells, and I knew I needed that! Crohn's Disease in Niemann—Pick Disease Type C1: Caught in the Cross—Fire of Host-Microbial Interactions | SpringerLink However, uncontrolled autophagy causes continual breakdown, such as muscle atrophy, which I was experiencing, and lysine is also needed to terminate autophagy to begin the regeneration process. In addition, lysine increases absorption of both iron and zinc, and a low iron level (anemia), with the fatigue that it causes, is a sign of lysine deficiency.

Vitamin D3 increases calcium absorption too, so I was told to take D3. But, I discovered that D3 needs to be activated by lysine in the vitamin D receptor, so this may be why people seem to need so much D3 these days. In addition, bone marrow cells that differentiate into bone, cartilage, and elastin can also differentiate into fat cells!-and people with osteoporosis have more fat cells in their bones. Adipocyte tissue volume in bone marrow is increased with aging and in patients with osteoporosis | SpringerLink This occurs when PPAR gamma is induced, for example, by insulin (from carbohydrates), linoleic acid, flaxseed oil, olive oil, and anthocyanins (in fruits and vegetables). This pretty much describes my diet at the time. In contrast, ketogenesis, as induced by lysine via PPAR alpha, prevents differentiation into fat, thus increasing bone mass. Activation of PPAR gamma in colon tumor cell lines by oxidized metabolites of linoleic acid, endogenous ligands for PPAR gamma - PubMed (nih.gov) https://pubmed.ncbi.nlm.nih.gov/ Consumption of oils and

anthocyanins may positively modulate PPAR-y expression in chronic noncommunicable diseases: A systematic review - PubMed (nih.gov)

I gave it a try one night and, strangely, after getting progressively worse for years, I noticed a very slight positive effect the next morning-that I felt a little more "together". So, I dove into research about lysine. But the first thing I found was that meat, fish, dairy, and eggs are the foods highest in lysine, while most of the foods that I was eating were very poor sources, especially since they were so high in arginine! I then remembered how several of my great grandparents and grandparents had lived long, healthy lives, to about ninety years old, eating the high lysine foods. After a great deal of research, I was convinced, completely changed to a high lysine diet, and, I'm very happy to say that I've recovered from most of my health problems.

So, I've compiled my research here to help others, with these topics:

- 1. How important lysine is for calcium, all hormones, and fertility, yet it's often low in the diet, plus it's depleted by toxins.
- 2. Lysine is needed to control arginine for strong and stable collagen, a functional immune system, and to prevent allergies, asthma, and pain.
- 3. Traditional diets, which emphasize meat, fish, dairy, and fermented grains, are higher in lysine than arginine.
- 4. A high lysine diet also helps to prevent obesity, diabetes, heart disease, cancer, and mental and neurological disorders.

CRITICAL IMPORTANCE OF LYSINE

Notably, lysine may be "the most important amino acid to determine protein needs"! This is because it's the essential amino acid that's too low in grains, which are higher in methionine, and people eat a lot of grains. Our foods are broken down into their amino acids, and enough essential amino acids are needed to make other proteins: enzymes, receptors, hormones, antibodies, neurotransmitters, etc. So, having an adequate amount of each of our enzymes, etc. depends on having enough lysine in the diet!

What was even more interesting was that the actions of many of these enzymes, etc. varied, depending on how the lysine contained in them is acted upon. Because of this, lysine "may be the major means by which signaling pathways modify protein behavior." Thus, adequate lysine is so fundamental to health that a study was entitled, "Why Always Lysine?"

REGULATES HORMONES This is also illustrated by the presence of a lysine at the catalytic, or regulating, site of many receptors, including nuclear receptors for all hormones, which affect and manage hundreds of bodily processes. <u>Nuclear receptor - Wikipedia</u> As seen from this long list, these receptors are commonly impaired:

Insulin

- PPAR alpha-induces ketogenesis, or fat burning
- All sex hormones
- Oxytocin-love, sociability, and mothering hormone
- Adrenal stress "fight-or-flight" hormones: cortisol, aldosterone, adrenaline, DHEA, and norepinephrine. These raise blood pressure, but lysine regulates them, normalizing BP.
- Vitamin A-fetal development, immune system, vision
- Vitamin D-lysine nuclear receptor is needed to activate D3 supplements.
- Thyroid hormone
- Dopamine-pleasure, satisfaction, and purposeful activity hormone (increased with lysine supplementation)
- SIRT-longevity hormone
- P53-fights cancer as the "guardian of the genome"
- PPAR alpha-ketogenesis: burns fat for energy, including for most of our heart energy
- Heme-detoxifies peroxynitrite, and forms hemoglobin for oxygen
- Cholesterol-receptor enables uptake into cells for cardiovascular and mental health

Not surprisingly then, lysine has been shown to help, or is deficient, with a wide variety of serious health problems. In fact, one reason for these health problems is that many chemicals specifically bind to lysine in these receptors, enzymes, etc. For example, when the catalytic lysine is impaired on the insulin receptor it causes insulin resistance. Mutagenesis of lysine 460 in the human insulin receptor. Effects upon receptor recycling and cooperative interactions among binding sites. (jbc.org) Insulin resistance is the fundamental problem of metabolic syndrome, which includes obesity, hypertension, diabetes, heart disease, and kidney disease. Link between Metabolic Syndrome and Insulin Resistance - PubMed (nih.gov) Thus, these chemicals are called obesogens. Obesogens and the Obesity Pandemic: A focus on prevention -YouTube Another example of chemicals binding to lysine is with the estrogen receptor, which causes breast cancer and infertility. The functional significance of nuclear receptor acetylation -PMC (nih.gov) These chemicals are also called estrogenic chemicals or endocrine disruptors. Importantly, they "include compounds to which the human population is exposed in daily life through their use in pesticides/herbicides, industrial and household products, plastics, detergents, flame retardants and as ingredients in personal care products." Endocrine <u>Disruptors and Obesity - PubMed (nih.gov)</u>

Chemicals that bind to lysine include pyrethroids, organophosphate pesticides (including Roundup, or glyphosate), bisphenol A, and the ubiquitous solvent trichloroethylene (for example, in degreasers and aerosol sprays used for crafts). Molecular determinants on the insect sodium channel for the specific action of type II pyrethroid insecticides - PMC (nih.gov)

Review of tyrosine and lysine as new motifs for organophosphate binding to proteins that have no active site serine - PMC (nih.gov Long-term exposure to a 'safe' dose of bisphenol A reduced protein acetylation in adult rat testes | Scientific Reports (nature.com) Acylation of protein lysines by trichloroethylene oxide - PubMed (nih.gov) Not surprisingly, these chemicals have been linked to disorders involving these receptors, such as fatty liver, obesity, diabetes, heart disease, kidney disease, mental illness, neurological disorders like multiple sclerosis,

Parkinson's, cancer, birth defects, miscarriages, and infertility. **Association Between Occupational Exposure to Pesticides and Cardiovascular Disease Incidence: The Kuakini Honolulu Heart Program** In addition, there's a poison in cottonseed oil that depletes lysine, which may be in cheap hamburgers from industrial dairy cows and in fish, as both are commonly fed cottonseed meal. This poison, called gossypol, binds to lysine in the cholesterol transporter, causing fatty liver, low hemoglobin, atherosclerosis, and dementia, and this poison "has a strong tendency to accumulate in animal tissues and is not easily cleared from the animal body. The response of meat ducks from 15 to 35 d of age to gossypol from cottonseed meal - ScienceDirect

FERTILITY Adequate lysine is required for synthesis and actions of sex hormones. Lysine is so important for fertility that it was featured in the movie "Jurassic Park", because the dinosaurs were infertile without lysine. So, toxins that bind to lysine cause infertility. Similarly, the cottonseed poison gossypol (from cottonseed meal in animal feed) binds to lysine in these enzymes and "inhibits steroid synthesis".

https://www.askjpc.org/vspo/show_page.php?id=cjhNcjZWbkN5L3UxQTdldzRER3ZTZz09

One way lysine determines fertility is that, in females, lysine is a catalytic amino in aromatase, which converts testosterone into estradiol. Aromatase Acetylation Patterns and Altered Activity in Response to Sirtuin Inhibition - PMC (nih.gov) Low enzyme activity causes high testosterone in females, with androgen-related polycystic ovarian syndrome symptoms of infertility, insulin resistance, facial hair, and increased muscle mass. https://pubmed.ncbi.nlm.nih.gov/9510005/ Lysine helps with these symptoms, so this may be via regulating aromatase. Another way lysine is needed for fertility is that lysine is the precursor to carnitine with its ketogenic effects, which has "immense" capabilities regarding fertility. Carnitine is low with both male and female infertility, and has been shown to help with both. https://ods.od.nih.gov/factsheets/carnitine-HealthProfessional/">https://ods.od.nih.gov/factsheets/carnitine-HealthProfessional/

Lysine and fertility is well-studied in farm animals, and lysine supplements are given to increase fertility, possibly due to the cottonseed meal they feed them. Giving lysine to cows also increases milk production, probably due to its function as oxytocin. Benefits of L-lysine & Ways to Avoid Its Deficiency | New Health Advisor (md-health.com) Oxytocin is also needed for erections, orgasm, and childbirth, and women have more oxytocin receptors than men. So, it's likely that a high lysine diet, especially as a ketogenic diet, would help humans with fertility and other male and female sexual disorders. Regarding child development, lysine improved appetite in poorly-thriving infants. Lysine Uses, Benefits & Dosage - Drugs.com Herbal Database

LYSINE IS NEEDED TO CONTROL ARGININE

A unique aspect of lysine is that the non-essential amino acid arginine needs to be lower than lysine in a diet. Arginine can be harmful because it's very high in nitrogen, but lysine controls its actions. Arginine also competes with lysine for entering cells. Lysine is also the most conserved amino acid as it's the last amino acid in the body to be broken down-not surprising, given these functions of lysine. Research Breakdown on Lysine – Examine

Common foods that are higher in lysine relative to arginine, in descending order: whey, other dairy, brewer's yeast, fish, avocado, pork, poultry, potato, beef, eggs, shellfish, and white, red, and black beans.

Common foods that are higher in arginine relative to lysine are, in descending order: tahini, orange juice, nuts, peanuts, berries and grapes, coconut, seeds, rice, corn, chocolate, gelatin/bone broth, wheat, oats, rye, peas, barley, chickpeas, soy isolate, quinoa, lentils, and tofu. Lentils and tofu are close to equal in both, which makes sense since they are so widely eaten.

COLLAGEN The need for more lysine than arginine is illustrated by how the body makes body whole, stable, and strong: by bringing lysine into the cell.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4572086/ Collagen needs to be strong and stable, and the related elastin needs to be elastic but strong. As components of skin, joints (cartilage), tendons, bone, hair and nails, muscles and heart, and the lining of the cardiovascular system (endothelium), collagen and elastin heal the body and literally hold the body together. Role of Collagen Wound Healing, hemostasis, wound debridement, phases (humanbiosciences.com) Collagen and elastin are also needed in eyes, ears, gums, the stomach lining, lungs, and the blood-brain barrier. So, my low lysine but high arginine diet might explain my distinct feeling of falling apart!

One problem with having more arginine than lysine is that the lysine transporter can also be used by arginine, if unoccupied by lysine. Then, the cell wall will no longer have lysine's stabilizing function, and becomes thin and "dramatically" deformed. This is because it's subject to "the special role played by Arg as an amino acid to bind to, disrupt and permeabilize lipid membranes." The Different Interactions of Lysine and Arginine Side Chains with Lipid Membranes - PMC (nih.gov) That "special role" of disrupting cell membranes is due to the high amount of nitrogen in arginine, which is converted to inflammatory nitric oxide. Inflammatory nitric oxide can be very harmful. For example, it makes nitrosamines which cause cancer, plus higher amounts "significantly boosted" COVID-19 and flu death.

ARGININE IS HIGH IN NITROGEN Arginine is very high in nitrogen, which is "highly reactive" and releases a large amount of energy. This is useful as human growth hormone for early growth and development, and it's the reason we put nitrogen in our garden-for rapid growth. It also explains why seeds of every sort, including grains, legumes, cocoa beans, and coconuts, are high in nitrogen-for rapid growth. But, keeping in mind the explosive nature of chemical nitrogen fertilizer (remember the deadly bombing of the Oklahoma City Federal Building), excessive nitrogen in the body can also become very harmful as inflammatory nitric oxide.

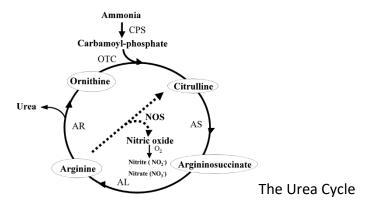
As a result, most of the arginine in our diet is degraded into urine and polyamines, which are also rich in nitrogen, or into collagen. This is useful when rapid repair is needed, such as for burn victims or with sepsis, and the lysine in the enzyme ornithine decarboxylase (OTC) directs this action. However, these polyamines are also the building blocks for pathogens, cancer cells, and

the brain parasite toxoplasma gondii. So, excessive availability of polyamines due to excessive dietary arginine, as a bountiful "terrain", causes them to replicate. This is why "targeting host arginine-associated metabolic pathways is an effective means of controlling viral replicative processes." Development and evaluation of a host-targeted antiviral that abrogates herpes simplex virus replication through modulation of arginine-associated metabolic pathways - PubMed (nih.gov)

Most amino acids have only 1 molecule of nitrogen, while arginine has four. This gives arginine the bitterness that you taste in unroasted nuts, seeds, chocolate, and grains. Lysine, on the other hand, has only two molecules of nitrogen, and tastes slightly sweet. Importantly, the body identifies bitterness as poison. So, our taste buds can sense that too much arginine relative to lysine is a problem. Furthermore, we often roast or bake these foods to high temperatures (284 degrees F) for "browning", to make them sweet. But, this causes carbohydrates to bind to lysine in what is called the "Maillard reaction", which turns lysine into harmful advanced glycation end-products. Examples of this are roasting peanuts and nuts, searing meat, and browning bread (the crust) and cheese (like for pizza). Adding sugar to baked or fried foods creates even more AGE's and lowers lysine further.

Most arginine is made in the body from citrulline, which is made from glutamate, the most abundant amino acid in the body. Arginine - Wikipedia The best food sources of citrulline are watermelon, watermelon leaves, cucumbers, pumpkin, pumpkin leaves, cantaloupe, and squash. Arginine is produced from citrulline right in the arteries and capillaries (vascular endothelial cells) to make a low level of nitric oxide for healthy blood flow. The body also produces arginine when we detoxify ammonia from excess nitrogen from other amino acids and breakdown of bodily proteins. Then we expel it as urine, in the kidneys. So, due to the abundance of nitrogen in the body, most dietary arginine is simply degraded. This was shown in a 4-week experiment with healthy adults where even arginine and arginine precursors, like glutamate, were eliminated from the diet, yet production of arginine in the body was unchanged. Furthermore, although it's often claimed that dietary arginine helps to detoxify ammonia, ammonia was adequately detoxified even without dietary arginine. So, dietary arginine adds disproportionately to the amount of nitrogen from amino acids to be detoxed. Importantly, degradation of arginine and oxidation of arginine (to inflammatory nitric oxide) were "markedly reduced" with no dietary arginine. Plasma arginine and citrulline kinetics in adults given adequate and arginine-free diets - PubMed (nih.gov) http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2574647/

ARGININE METABOLISM The high amount of nitrogen in arginine is extremely important for proper blood flow with endothelial nitric oxide and neuronal nitric oxide for blood flow to the brain. Nitrogen is a powerful growth factor, so arginine that we make is also used for making growth hormone, especially needed during development, for wound healing, and in older adults. Along these lines, premature infants need slightly more arginine than lysine-for growth hormone-as they can't synthesize arginine. But, once full term, infants need more lysine, and mother's milk is higher in lysine than arginine.



ARGININE MADE IN THE BODY Most arginine present in the body is produced in the body. Lysine recycles nitrogen by blocking arginase, redirecting endogenous arginine to healthful constitutive nitric oxide and citrulline, which then becomes arginine again. In the case of infection, inflammatory NO (induced by bradykinin, for example) is used to destroy pathogens, but this also causes damage. So, once the pathogen is destroyed, lysine stops inflammatory NO by signaling for debris clean-up by macrophages via the OAT enzyme. OAT also degrades arginine into ornithine and then into collagen for repair. So, when lysine is adequate, the high amount of nitrogen in arginine is beneficial rather than harmful: it causes healthy relaxation of arteries for proper blood flow as endothelial nitric oxide, plus it fights infections as inflammatory nitric oxide, and then it repairs the body!

Healthful nitric oxide is induced in blood vessels by the hormone prostacyclin from the essential fat arachidonic acid, which prevents blood clots from forming, but healthful nitric oxide is low with many diseases. This lowers oxygenation, and occurs if lysine is unavailable to block arginase and to maintain endothelial function, as when toxins bind to lysine. In this situation, inflammatory nitric oxide is induced instead by bradykinin, an "inflammatory peptide", and inflammatory NO is increased by dietary arginine.

For example, arginase is overactive with rheumatoid arthritis (RA) and arginase breaks down endogenous arginine as well as dietary arginine, causing low constitutive nitric oxide. At the same time, inflammatory nitric oxide and bradykinin are high with RA: when nitric oxide is "overproduced by physiological disorders, severe inflammatory diseases such as rheumatoid arthritis can occur." Arginase levels are increased in patients with rheumatoid arthritis - PubMed (nih.gov) Role of the eNOS Uncoupling and the Nitric Oxide Metabolic Pathway in the Pathogenesis of Autoimmune Rheumatic Diseases (hindawi.com) Soluble CD13 induces inflammatory arthritis by activating the bradykinin receptor B1 - PubMed (nih.gov) So, rather than needing more arginine in the diet for healthy blood flow, as had been promoted, more lysine provides healthful blood flow from endogenous arginine, as well as a strong immune response when needed.

KIDNEYS AND AMMONIA When excessive dietary arginine is disposed of as urea it can cause gout. In contrast, high lysine dairy products are associated with low uric acid, so there's less risk for gout. Interestingly, vegans, with their high arginine diet, have higher uric acid than meateaters, although evidence is mixed. Also, high arginine soy milk increased uric acid. Gout and

<u>Plant-Based Diets – Vegan Health</u> So, a high arginine diet may interfere with the kidneys' disposal of uric acid in the urea cycle.

Evidence for this is the harmful effects that arginine supplementation has on the kidneys. Chronic long-term supplementation with arginine increases mTOR, thus aging the kidney and causing functional decline. Frontiers | Detrimental Effects of Chronic L-Arginine Rich Food on Aging Kidney (frontiersin.org) Arginine supplementation also caused kidney fibrosis, which occurs with end-stage kidney disease, and shortened life-span in mice with lupus. L-arginine supplementation accelerates renal fibrosis and shortens life span in experimental lupus nephritis - PubMed (nih.gov) Also, an important function of uric acid is to detoxify peroxynitrite, the free radical made from excessive dietary arginine during inflammation. So, more uric acid would be needed with a high arginine diet.

https://www.sciencedirect.com/science/article/abs/pii/S0306987700911186

When the urea cycle isn't functioning properly, ammonia builds up in the muscles and brain. Elevated blood ammonia is found with cigarette smoking, high blood sugar, heavy exercise, stress (raised cortisol). Elevated ammonia leads to both mental and physical symptoms, such as insomnia, headaches, confusion, inability to concentrate, low body temperature, drowsiness, lack of coordination, shortness of breath, combativeness, muscle stiffness and weakness, lethargy, low serotonin, enlarged liver, tremor, blurry vision, and anorexia. AMMONIA TOXICITY: Part 1 - NutriStart Many diseases are characterized by high ammonia levels, such as rheumatoid arthritis, Lyme disease, Alzheimer's, MS, ALS, autism, diabetes, ADHD, autism, schizophrenia, Lyme disease, Parkinson's, alcoholism, poorly functioning liver, anorexia, OCD, and congestive heart failure. Furthermore, during the inflammatory immune response, excess ammonia increases production of inflammatory NO by contributing more nitrogen. Effects of acute ammonia toxicity on nitric oxide (NO), citrulline-NO cycle enzymes, arginase and related metabolites in different regions of rat brain - PubMed (nih.gov)

IMMUNE SYSTEM

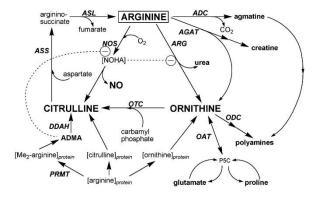
A high lysine diet is crucial for a functioning immune system. Lysine increases natural killer cell activity and regulates the inflammatory immune response. For example, it's needed to inhibit inflammatory tumor necrosis factor and interferon. Lysine also is needed for functional exosomes, which are tiny proteins that are sent to immune system components in response to a toxin, in order to activate it. Exosomes are nearly identical to viruses, so some think that viruses are in fact exosomes, and others think that viruses use exosomes to enter cells as a kind of "Trojan horse". Either way, lack of lysine might cause these unusual exosomes to be dysfunctional, plus these exosomes, which we call viruses, are replicated via polyamines from arginine. In fact, much of lysine's immune system function comes from how it controls the production and action of arginine: "Lysine exerts antagonistic actions against arginine via several proposed mechanisms: serving as an antimetabolite of arginine, enhancing the excretion of arginine by competing for reabsorption at the renal tubule, competing for

intestinal absorption, inducing arginase to break down arginine, and competing for transport into cells." Gaby 2006

Lysine is best known for controlling herpes viruses/exosomes, which survive and replicate in the presence of excessive dietary arginine, and people with herpes are advised to follow a high lysine diet. Relation of arginine-lysine antagonism to herpes simplex growth in tissue culture - PubMed (nih.gov) Two people were listening to a talk I gave on lysine and arginine. They told me that they took arginine one night, and each one woke up the next morning with cold sores! They didn't even know that they had herpes.

Herpes cold sores are also triggered by chocolate, peanut butter, nuts, seeds, and coconut, which have the highest arginine to lysine ratio. <u>Best and Worst Foods for Herpes</u> (<u>ondietandhealth.com</u>) There are many in this family: simplex 1/2, Epstein Barr, zoster (chicken pox/shingles), HPV, and cytomegalovirus. Herpes viruses, especially Epstein Barr, are found with a wide range of problems, like autoimmune diseases, hypertension, Alzheimer's, schizophrenia, birth defects, autism, and cancers. So, chocolate, peanut butter, etc. should probably be avoided with these problems.

Moreover, studies have found that pretty much all pathogens are dependent on arginine. This is because these pathogens degrade it into polyamines, plus they convert arginine into growth hormone. For just two examples, pneumonia-causing streptococcus and the common brain parasite, toxoplasma gondii, are arginine dependent. Regulation of Arginine Acquisition and Virulence Gene Expression in the Human Pathogen Streptococcus pneumoniae by Transcription Regulators ArgR1 and AhrC - Journal of Biological Chemistry (jbc.org) Toxoplasma gondii lacks the enzymes required for de novo arginine biosynthesis and arginine starvation triggers cyst formation - PubMed (nih.gov) I used to get bad colds several times a year, even had pneumonia twice, and streptococcus pneumoniae bacteria are found in abundance with these problems. But now the only times I've been sick are when I've gone off the diet. Also, toxoplasma is a serious problem as it has been linked to nearly all mental and neurological disorders, vision problems, rheumatoid arthritis, cancer, diabetes, and more.



Arginine Metabolism: Boundaries of Our Knowledge,, - ScienceDirect

Arginine polyamines and growth hormone (as converted into insulin-like growth factor) also feed cancer cells. In fact, "arginine is the most consumed amino acid in the inner necrotic core of tumor mass, indicating its high demand for the survival of tumor cells". Cancers | Free Full-Text | Arginine Signaling and Cancer Metabolism (mdpi.com)

ARGINASE One critical immune function of lysine is that it inhibits the enzyme arginase (ARG in diagram), which serves a number of functions. 1. Inhibiting arginase recycles the nitrogen in arginine to become healthful nitric oxide rather than being expelled, and wasted, as urine via ARG, plus this makes citrulline to form arginine again. This also avoids formation of polyamines and cell proliferation, as well as excessive glutamate via ARG. 2. In the case of infection, arginine becomes inflammatory nitric oxide to destroy the pathogen, rather than being degraded into polyamines, which feed the infection instead! 3. Lysine-generated inflammatory nitric oxide is controlled, whereas, with excessive dietary arginine, inflammatory nitric oxide reacts with superoxide to form peroxynitrite, which uncouples oxidative phosphorylation (energy generation), damages DNA, and is found with many if not all serious diseases. Nitric oxide and oxygen radicals in infection, inflammation, and cancer - PubMed (nih.gov) One function of ketones, which are critical for health, is to inhibit arginase. In addition, many medications block arginase: heart disease and kidney disease meds, and the "wonder drug" diabetes medication-Metformin. For wound healing and regeneration, lysine doesn't inhibit arginase but, instead, uses ornithine to make proline for collagen, via the OAT enzyme. Lysine-induced OAT also prevents the enzyme ornithine decarboxylase from producing polyamines from arginine. OTC also is regulated by lysine. Lysine 88 Acetylation Negatively Regulates Ornithine Carbamoyltransferase Activity in Response to Nutrient Signals - PMC (nih.gov)

H. PYLORI Arginine metabolism with H. pylori illustrates the problem of excess dietary arginine without lysine to inhibit arginase. Most dietary arginine is degraded, while lysine would have redirected that arginine to become inflammatory nitric oxide to destroy it! So, arginine metabolism "leads to H. pylori-induced DNA damage and immune dysregulation through polyamine-mediated oxidative stress and impairment of antimicrobial nitric oxide synthesis", which then leads to "gastritis, ulcer disease, and gastric cancer". Arginine and Polyamines in Helicobacter pylori-Induced Immune Dysregulation and Gastric Carcinogenesis - PMC (nih.gov) Thus, the old remedy of drinking high lysine milk for an ulcer might help along these lines.

Excess nitric oxide can become peroxynitrite which, due to the damage it causes, increases pathogen entry into cells. In contrast, adequate lysine in cellular collagen prevents viruses and bacteria from entering cells, plus lysine controls dietary arginine. So, it's best to limit arginine and increase lysine, that is, have a high lysine diet, for all pathogens.

ARGININE SUPPLEMENTS

In the recent past, supplemental arginine was heavily promoted as fountain of youth for older people-for life extension, to increase bone density and muscle mass, and to increase nitric oxide for cardiovascular health. However, studies have found that arginine supplements raise growth hormone (low in the elderly) only in young people. Also, lysine is important muscles and bones.

Regarding heart health, "Short term L-arginine supplementation enhances endothelial NO production, while long-term supplementation causes endothelial senescence (deterioration with age)"! Long term exposure to L-arginine accelerates endothelial cell senescence through arginase-II and S6K1 signaling. - Abstract - Europe PMC

Taking arginine as a supplement does lower blood pressure. L-arginine: Does it lower blood pressure? - Mayo Clinic However, this is no longer recommended as it might lower it too much. Moreover, in an inflammatory situation, excessive arginine joins with bradykinin to become desarginine9-BK, which becomes inflammatory nitric oxide. This lowers blood pressure in a destructive way-by causing blood vessels and capillaries to become permeable. Kallikrein-kinin blockade in patients with COVID-19 to prevent acute respiratory distress syndrome - PMC (nih.gov) https://pubmed.ncbi.nlm.nih.gov/1659406/ This causes veins to constrict, so capillaries leak, and leaky capillaries can cause swelling, or edema, which is a possible side effect of arginine supplementation. Bradykinin - Wikipedia

Moreover, people who would take arginine to lower blood pressure may already be taking medications that affect the bradykinin system, such as ACE-inhibitors and Losartan, diabetes meds like Metformin, and diuretics. Metformin as a prevention and treatment for preeclampsia: effects on soluble fms-like tyrosine kinase 1 and soluble endoglin secretion and endothelial dysfunction - PubMed (nih.gov) As a result, people who take these medications are warned against taking arginine.

Arginine has been highly recommended for years to increase athletic performance because arginine is used to make creatine for muscles, and endothelial nitric oxide is desired for greater pumps. However, it's now known that only endogenous arginine, and not dietary arginine, is used for making creatine. Furthermore, "numerous studies have shown that orally supplemented l-arginine, even when dosed as high as 6g/day, has no benefit on nitric oxide production or athletic performance."

https://advancedmolecularlabs.com/blogs/news/research-report-current-controversy-pre-workout-supplements

Instead, healthful nitric oxide is produced from endogenous arginine, which is made from citrulline. So, muscle builders are now advised to take citrulline instead of arginine for creatine and nitric oxide. Also, carnitine from lysine improves exercise performance, and there's a "rapid" conversion of lysine to carnitine. Carnitine is a form of the ketone beta hydroxy-butyrate, and ketones power the muscles and heart. This conversion also yields glycine, which is needed for collagen and muscle. Also, supplemental lysine is "rapidly transported to muscle tissue, and within 5 to 7 hours following ingestion is highly concentrated in the muscle". Tomblin 2001 So, this may be why lysine is highly recommended for "peak performance". The Benefits of a Lysine Supplement For Athletes - Quantum Health

Importantly, arginine is given to mice to study necrotizing pancreatitis, and there's a report of a body builder who developed pancreatitis from taking arginine! The second case of a young man with L-arginine-induced acute pancreatitis - PubMed (nih.gov) Acute pancreatitis possibly due to arginine use: a case report - PubMed (nih.gov) Chronic pancreatitis damages insulin-

producing beta cells, so it can lead to diabetes. In one study, after inducing pancreatitis with arginine, they cured the mice with lysine! <u>Suppression of acute pancreatitis by L-lysine in mice - PMC (nih.gov)</u> Furthermore, lysine increased glutathione, the most powerful antioxidant in the body, catalase (low catalase causes grey hair!), and vital anti-oxidant superoxide dismutase! So lysine is important for the most important anti-oxidants-those made in the body.

Arginine is still recommended for erectile dysfunction and for increasing testosterone. It does cause erections, but it doesn't increase testosterone in the long term. <u>L-Arginine for Testosterone - Supplements in Review</u> On the other hand, "Inhibition of inflammatory nitric oxide (which arginine supplements would increase!) displayed beneficial effects in the treatment of ED." This is what lysine does. In addition, arginine increases and sustains high IGF-1, which is linked to development of prostate cancer! https://pubmed.ncbi.nlm.nih.gov/15562830/

Despite the clear negative long-term results regarding prostate health, arginine and high arginine nuts and seeds are still promoted for ED and for prostate health in general. Based on a 2016 study, nuts are even recommended for prostate cancer survival. However, the nut study was funded by the International Tree Nut Council Nutrition Research & Education Foundation and was conducted by avid vegan and nut promoter Walter Willett, so the diagnostics may be questionable. Nut consumption and prostate cancer risk and mortality - PMC (nih.gov)

Other side effects from arginine supplementation include heart palpitations, dizziness, light-headedness, irritability, depression, anxiety, dehydration, headache, restless legs, indigestion: bloating, GERD, swollen legs (edema), chest pain, low blood sugar, lower back pain, breathing problems, blood abnormalities, asthma, raises homocysteine, worsened kidney disease, worsened sickle cell disease.

ALLERGIES AND ASTHMA

Histamine normally induces nitric oxide for a very short while, but NO can become excessive, causing breathing difficulty, anaphylaxis, hives, angioedema, eczema, sinus congestion, and headache. https://pubmed.ncbi.nlm.nih.gov/12707234/ Medications that relieve these symptoms-epinephrine, Benadryl, and corticosteroids-work by increasing endothelial nitric oxide (epinephrine and Benadryl), or inhibiting nitric oxide synthase (corticosteroids), both of which lower inflammatory NO. <a href="mailto:Epinephrine regulation of the endothelial nitric-oxide synthase: roles of RAC1 and beta3-adrenergic receptors in endothelial NO signaling - PubMed (nih.gov) (PDF) Cilia Stimulatory and Antibacterial Activities of T2R Bitter Taste Receptor Agonist Diphenhydramine: Insights into Repurposing Bitter Drugs for Nasal Infections (researchgate.net) Inducible Nitric Oxide Synthase and Proinflammatory Cytokine Expression by Human Keratinocytes during Acute Urticaria | Molecular Medicine | Full Text (biomedcentral.com) Not surprisingly then, arginine supplementation worsens allergies and asthma, because it increases histamine release from mast cells, with its accompanying nitric oxide. L-arginine - Mayo Clinic Effect of arginine analogues on rat hind paw oedema and mast cell activation in vitro - ScienceDirect

On the other hand, lysine's role in increasing healthful nitric oxide, as well as lowering adrenal stress hormones, would lower histamine release. Nitric oxide: a regulator of mast cell activation and mast cell-mediated inflammation | Clinical and Experimental Immunology | Oxford Academic (oup.com) Interestingly, histamine is a very small molecule but it's particularly high in nitrogen-no wonder it can cause so many problems! For myself, I would get eczema on my hands every time I had cow milk in any form, so I always had goat milk instead. After several years on a high lysine diet, also supplementing lysine, I no longer got eczema when I had cow milk products! To be fair, I also gave up sugar and went on a ketogenic diet, so that might have had a lot to do with it. But the important thing is: no more eczema!

PAIN

Arginine supplements help with the extreme pain of Complex Regional Pain syndrome, but excessive arginine can also increase pain in a number of ways.

- Muscles: Delayed muscle soreness from exercise is due to nitric oxide." Along these lines, with an inflammatory condition, nitric oxide, with its damage due to peroxynitrite, causes pain. Thus, in mouse studies, inhibitors of inflammatory NO have been found to help with pain and inflammatory and neuropathic pain, as well as "endotoxemia, sepsis, heart failure, depression, neurodegenerative disorders, epilepsy, and arthritis," although no NO inhibitor has been developed for humans.
 https://www.sciencedirect.com/science/article/abs/pii/S1089860311005052
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- Shingles pain, from the chicken pox herpes virus, can be very intense and is related to dietary arginine. "Arginine deficiency suppressed herpes simplex virus replication in tissue culture. Lysine, an analog of arginine, as an antimetabolite, antagonized the viral growth-promoting action of arginine. The in vitro data may be the basis for the observation that patients prone to herpetic lesions and other related viral infections, particularly during periods of stress, should abstain from arginine excess and may also require supplemental lysine in their diet." Relation of arginine-lysine antagonism to herpes simplex growth in tissue culture PubMed (nih.gov)
- Osteoarthritis: "NO (nitric oxide) plays a catabolic (destructive) role in the development
 of OA and mediates the inflammatory response, is involved in the degradation of matrix
 metalloproteinases, inhibits the synthesis of both collagen and proteoglycans, and helps
 to mediate apoptosis. NO and its derivatives have a similarly complicated involvement in
 nociception and pain, which may contribute to the functional disability of OA."
- "Intradermal administration of L-Arginine causes a dose-dependent enhanced sensitivity to pain." Thus, "The development of iNOS inhibiting therapeutic agents in the treatment of pain is very promising."
- Side effects from supplemental arginine include lower back pain, chest pain.

When I was eating my high arginine diet and became disabled, I was suffering from many of these side effects: a lot of pain, bloating and GERD, restless legs, depression, heart palpitations, dizziness and low blood sugar, frequent urination, allergies, and breathing problems. Regarding

breathing problems, the biggest triggers of anaphylaxis are peanuts and nuts, also sesame seeds and chickpeas in other countries, and, of the foods higher in arginine than lysine, peanuts, nuts, sesame seeds, and chickpeas are the highest in arginine!

I actually ate more nuts and seeds before my injuries, in the effort to feel better. After all, they're "super-foods" since they're high in antioxidants, and I needed super-healthy foods. This is the "food as medicine" way of thinking. However, focusing on medicinal actions of a few constituents of foods, without the context of our ancestral diet, which are the foods our bodies evolved on, can't be reliable. Now I prefer to trust the wisdom of my ancestors, as explained in the next section, rather than the current state of nutritional science. And, now that I completely avoid these supposed "superfoods", I feel far better!

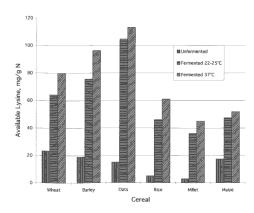
A HIGH LYSINE DIET IS ALL ABOUT TRADITIONAL FOODS

Lysine is readily available in protein foods, so it may not seem to be difficult to get enough, especially if you're eating meat, fish, and dairy products. Yet, for a number of reasons, you may not be consuming adequate lysine, which is 30 mg per kg. Plus, this requirement may be too low, given the many toxins that bind to lysine.

Traditionally, people have included dairy products and/or fish, which are the foods highest in lysine, in their regular diet, but both foods are eaten far more in European countries than in the U.S. In Japan, where they eat little dairy but a lot of grains, fish consumption is 3 times higher than in the U.S. Also, many people are eating more high arginine foods in recent times, with the emphasis placed on whole grains, legumes, nuts, seeds, peanut butter, and dark chocolate, and with the encouragement from the medical establishment to cut back on meat and dairy products.

A traditional practice that increases lysine in the diet is to ferment high arginine foods. Traditionally, wheat, rye, millet, rice, and quinoa were ground to a flour, then fermented for many hours. Examples are sourdough bread, South Indian rice pancakes and African teff or millet breads. However, in modern times, we prepare wheat with little or no fermentation, for bread, pizza, pasta, pitas, muffins, crackers, and desserts.

Some legumes-red, black, and white beans-are higher in lysine than arginine, and lentils are about even. In addition, all of these foods contain trypsin-inhibitors, which block absorption of lysine, and modern wheat has been bred to have even more trypsin-inhibitors to protect them from insects. Trypsin inhibitors are broken down during traditional fermentation, so lysine becomes more available for digestion from these foods. Fermenting bacteria also produce lysine, so lysine is increased over 5-fold in oats when fermented at 98.6 degrees F.! It's no wonder that people have traditionally prepared their low lysine foods in this way.



Source: World Health Organization

Danish foods are a good illustration of how traditional diets are higher in lysine than arginine. Split peas are much higher in arginine than lysine, so, between soaking and cooking, it takes three days to prepare Danish pea soup! Danes also cook the peas with a ham bone for some high arginine collagen, but then add plenty of ham-for a beautifully balanced soup.

Similarly, rye has the best lysine to arginine ratio of the grains, and sourdough rye bread, which most Danes still make a home, is a highly revered tradition. They ferment it for about 12 hours, slice it thin, and spread it with enough butter that you can see your teeth marks in it-tandsmør! This bread is the basis for open-face sandwiches, called smørrebrød, served with a large variety of high lysine toppings, like ham, shrimp, beef, or their favorite-liver pate and beet pickles. So, a high lysine diet is as delicious as it is nutritious. More evidence for a high lysine diet, with few plant foods eaten, comes from a paleolithic site in Sweden. Their food was mainly fish, and then meat, with mushrooms, berries, and nuts making up a "meagre" 3% of their protein. Nordic Stone Age diet was dominated by fish (sciencenordic.com)

Given the great importance of lysine, together with the potential harm of too much arginine, it made sense to me that the high lysine protein foods, including potatoes, were the basic foods of my Northern European ancestors, like my great grandparents, three of whom lived active lives until their "final sickness" around age 90. Even the foods I grew up with were still either high in lysine or at least balanced equally, like chicken soup, which is counted as the national soup for many countries around the world. Chicken is very high in lysine, while the gelatin in broth is high in arginine. So, together, it's a balanced dish. Also, in countries where they eat a lot of grains, like Russia and India, they eat fermented dairy at every meal. So, I substituted meat for peanut butter and nuts, and cut way back on legumes and bread, and began to feel like I might recover.

Digestion of all foods is affected by the lysine to arginine balance, as lysine and arginine have different effects on the digestive system, weight, blood sugar control, and heart health.

OBESITY

Metabolic health is our ability to convert food into energy, including our ability to make ketones for heart energy. Insulin resistance lowers the ability to make energy, so it's an important cause of metabolic syndrome, and the major manifestation of metabolic syndrome is coronary artery disease. Metabolic Syndrome and Insulin Resistance: Underlying Causes and Modification by

<u>Exercise Training - PMC (nih.gov)</u> Metabolic syndrome also includes diabetes, fatty liver, and kidney disease. Lysine deficiency is fundamental problem with metabolic syndrome, insulin resistance, and coronary artery disease.

Lysine is important for digestive health and, especially as carnitine, for maintaining a healthy weight. It's needed to absorb minerals, and its anti-inflammatory action improves diarrhea, leaky gut, and irritable bowel syndrome. Effect of lysine supplementation on health and morbidity in subjects belonging to poor peri-urban households in Accra, Ghana | The American Journal of Clinical Nutrition | Oxford Academic (oup.com) Anti-inflammatory Effects of Poly-L-lysine in Intestinal Mucosal System Mediated by Calcium-Sensing Receptor Activation - PubMed (nih.gov) Hypothyroidism is common with metabolic syndrome, and lysine increased thyroid hormone in the elderly. This essential lysine (fit-leader.com)

In contrast, arginine turns into glucose, and induces insulin production (which signals for fat storage) from the pancreas more than other amino acids. As a result, arginine decreases satiety, thus increasing meal frequency. Meal Pattern of Male Rats Maintained on Amino Acid Supplemented Diets: The Effect of Tryptophan, Lysine, Arginine, Proline and Threonine - PMC (nih.gov) On my ketogenic diet, I often eat a Wasa cracker covered with 2 tablespoons of butter 2 hours before a meal, along with a ketogenic tea. This increases my ketones by 0.2, so I get plenty of energy and don't feel like eating. As an experiment, I tried eating a high arginine keto fat bomb of MCT oil, peanuts, and chocolate, with 6 grams of fat. My ketone level stayed the same, and I was hungry in 45 minutes! I did this twice, and had planned to try it a third time, but I missed my satisfying and energy-giving butter snack too much.

Notably, lysine is one of only two amino acids that are degraded exclusively into ketones (burn dietary and body fat for energy) instead of glucose. When supplemented, lysine "rapidly" turns into carnitine, which is a "potent" inducer of ketosis as it contains a ketone, which reduces belly fat and lowers cholesterol (by burning it for energy). In addition, lysine is the catalytic amino acid for activating PPAR alpha, which induces ketogenesis. These functions may be why lysine deficiency causes fatigue.

Ketones are the primary energy source for the heart so, in a study, heart patients were given lysine, carnitine, and other supplements to treat arrythmia, which is "common" after age 65, by generating ketones. After 6 months, 48% were free of episodes and 70% had improvements in their heart condition. Arrhythmia - Dr. Rath Research Institute (drrathresearch.org) In addition, lysine is needed for longevity protein SIRT1, which is low with obesity and heart disease, as shown regarding thyroid hormone regulation. SIRT1 Regulates Thyroid-Stimulating Hormone Release by Enhancing PIP5Ky Activity through Deacetylation of Specific Lysine Residues in Mammals - PMC (nih.gov) So, increasing SIRT1 by a ketogenic diet (which is high in lysine: dairy, fish, and meat) is a tool used for managing metabolic syndrome and heart disease. Ketogenesis and SIRT1 as a tool in managing obesity - PubMed (nih.gov)

DIABETES

Lysine is an "effective therapy" for diabetes. Lysine increased diabetics' insulin receptor enzyme activity, which lowered their blood sugar by 27%. https://pubmed.ncbi.nlm.nih.gov/11886082/
This may be due to lysine's presence at the site of the insulin nuclear receptor. Similarly, "Lysine ingested with glucose dramatically attenuated the glucose-stimulated glucose response (in healthy volunteers)." https://link.attenuates.he.glucose-response-to-ingested_glucose_without-a-change-in-insulin response-left-healthy-therapy">https://link.attenuates.he.glucose-response-to-ingested_glucose_without-a-change-in-insulin response-left-healthy-therapy">https://link.attenuates-the-glucose-response-to-ingested_glucose-without-a-change-in-insulin response-left-healthy-therapy
https://creativecommons.new.org/<a href="h

Hemoglobin detoxifies inflammatory nitric oxide but, when it isn't detoxified quickly enough, the free radical peroxynitrite is formed. Reaction of Human Hemoglobin with Peroxynitrite - Journal of Biological Chemistry (jbc.org) This causes much damage with both type 1 and type 2 diabetes, leading to complications for 50% of diabetics. Peroxynitrite-Driven Mechanisms in Diabetes and Insulin Resistance – the Latest Advances - PMC (nih.gov) So, adequate functional hemoglobin is essential. One problem with diabetes is that hemoglobin becomes glycated, or covered with sugar from high blood sugar, while lysine maintains functional hemoglobin by preventing hemoglobin glycation, or high HbA1c. In addition, lysine is needed for functional hemoglobin since lysine is the nuclear receptor for heme. L-lysine supplementation improved glycemic control, decreased protein glycation, and insulin resistance in type 2 diabetic patients | SpringerLink Nuclear receptor - Wikipedia Thus, "3 grams of lysine per day inhibited protein (hemoglobin) glycation, improved glycemic control, and increased antioxidant markers in type 2 diabetic patients. This is very important, as a high HbA1c score is one of the highest risk factors for COVID-19 deaths. Haemoglobin A1c is a predictor of COVID-19 severity in patients with diabetes - PubMed (nih.gov)

https://link.springer.com/article/10.1007/s13410-021-00931-x Similarly, lysine prevented the formation of advanced glycation end products. Lysine Uses, Benefits & Dosage - Drugs.com Herbal Database

Fatty liver is very serious as it's both a consequence and a cause of diabetes. Notably, lysine plus DHA ameliorated fatty liver, in part by inducing ketosis. Lysine supplementation, with corn as the sole protein source, also prevented fatty liver in rats. Enhanced Amelioration of High-Fat Diet-Induced Fatty Liver by Docosahexaenoic Acid and Lysine Supplementations - PMC (nih.gov) Cataracts are another common complication of diabetes, and lysine prevented diabetic cataract formation. Beneficial effect of lysine and amino acids on cataractogenesis in experimental diabetes through possible antiglycation of lens proteins - PubMed (nih.gov) Also, "Bendazac lysine was tested for treating diabetic neuropathy, and it improved many markers, such as HbA1c, blood glucose, insulin levels, advanced glycation end-products, and anti-oxidants in nerves." https://pubmed.ncbi.nlm.nih.gov/17184506/

THE WONDER DRUG Metformin is the most widely prescribed diabetic drug in the world, prescribed to more than 150 million people, and is the most-prescribed drug in the U.S.! Metformin is called a "wonder drug" because, not only is it the first-line medication for type 2 diabetes, it's also prescribed for prediabetes, polycystic ovarian syndrome, and schizophrenia (for weight gain). In addition, it helps with breast, colon, and prostate cancer, dementia, stroke,

lowers viral load, asthma (arginase is high with asthma), increases life span, and psoriasis. It's even given to children as young as six years old! Is metformin a wonder drug? - Harvard Health

Metformin does three major things, which lysine happens to do as well. 1. It induces ketosis, which reduces the production of glucose after a meal, and supplies the energy that diabetics can't produce from glucose. 2. Metformin also blocks arginase, so it improves blood flow. PPARα-Dependent Modulation by Metformin of the Expression of OCT-2 and MATE-1 in the Kidney of Mice - PubMed (nih.gov) 3. Metformin blocks the enzyme ornithine decarboxylase, thus blocking the degradation of dietary arginine into polyamines. Many pathogens also have this enzyme to produce their required polyamines from dietary arginine. So, blocking ODC reduces polyamines from arginine, lowering viral load and helping with cancer. https://pubmed.ncbi.nlm.nih.gov/33915902/

The main side effect of Metformin is stomach upset, which can cause poor compliance. Also, diabetics commonly develop moderate chronic kidney disease, and the actions of Metformin damage the kidneys further. Effect of metformin on kidney function in patients with type 2 diabetes mellitus and moderate chronic kidney disease - PMC (nih.gov) This may be because, like arginine, Metformin is very high in nitrogen, for, as a bi-guanide, it's related to guanine, made from bat guano. As a result, one of its side effects is that it increases nitrogen in urine (a high BUN test), which normally indicates kidney damage.

Lysine, on the other hand, "diminished development of hypertension and kidney injury (in rats with hypertension and kidney disease). Protective mechanisms include diuresis, further acceleration of lysine conjugate formation, and inhibition of tubular albumin uptake."

Accelerated lysine metabolism conveys kidney protection in salt-sensitive hypertension | Nature Thus, the benefits from this "wonder drug" also illustrate the wonders of lysine, especially as part of a high lysine ketogenic diet, that has only good side effects!

HEART DISEASE

Adrenal stress hormones raise blood pressure, and lysine is needed to keep these hormones at a healthy level. Thus, lysine was found to normalize blood pressure as increased by aldosterone. I-Lysine Acts as a Serotonin Type 4 Receptor Antagonist to Counteract In Vitro and In Vivo the Stimulatory Effect of Serotonergic Agents on Aldosterone Secretion in Man - PubMed (nih.gov) Also, just one gram of lysine per day normalized blood pressure in men and women who had 'sub-optimal lysine intake" due to a high grain diet. This is possibly similar to many in the U.S. at this time. Effect of lysine supplementation on hypertensive men and women in selected peri-urban community in Ghana BMC Nutrition | Full Text (biomedcentral.com)

Another heart-protective role of lysine is seen with LDL cholesterol. "Elevated plasma Lp(a) cholesterol, which has a lysine-binding site, is an independent risk factor for cardiovascular disease", elevating risk by 70%. Impact of apolipoprotein(a) isoform size heterogeneity on the lysine binding function of lipoprotein(a) in early onset coronary artery disease - PubMed (nih.gov) Lp(a) is called "sticky" cholesterol, which can turn into plaques. But, when lysine is

absorbed into it, they become normal LDL! Furthermore, lysine converts cholesterol into bile, thus controlling LDL cholesterol and preventing fatty liver. https://pubmed.ncbi.nlm.nih.gov/1486246/

Lysine is essential for endothelial health, and "endothelial function is the key to cardiovascular health". Robert Furchgott (jewishvirtuallibrary.org) How Caffeine and L-Arginine Combination Affects Your Cardiovascular System. A CytoSolve Systems Biology Analysis. (vashiva.) com Endothelial permeability and dysfunction is an early marker for heart disease, and causes blood clots, hypertension, and angina. Taking lysine as a supplement has been recommended for heart disease since the 1970's, when Linus Pauling found that taking 6 grams of lysine, combined with 3-18 grams of vitamin C, gave quick relief from angina. https://cardiacos.net/wp-content/uploads/ArticulosMedicos/20170813/2004---Heart-cure.pdf In another study, people with heart failure were given a multi-nutrient treatment that included lysine, and they had improvements in fatigue, shortness of breath, and swollen ankles. The researchers called out lysine's role in making collagen as crucial for the protection of the endothelium of the artery walls. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4572086/ Similarly, loss of elastin in arteries increases risk for hypertension, heart attack, heart failure and stroke. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4572086/ Similarly, loss of elastin in arteries increases risk for hypertension, heart attack, heart failure and stroke. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4572086/ Similarly, loss of elastin in

In sharp contrast, researchers tested whether 9 grams of arginine per day would help people who had already had a heart attack. It would make sense that taking arginine would prevent another heart attack because blood pressure is elevated during a heart attack, and supplemental arginine lowers blood pressure by dilating blood vessels. Also, uncontrolled high blood pressure causes heart attacks. However, this study ended tragically because the only people who had another heart attack, and died, were six people who had taken the arginine! L-Arginine Therapy in Acute Myocardial Infarction: The Vascular Interaction With Age in Myocardial Infarction (VINTAGE MI) Randomized Clinical Trial | Acute Coronary Syndromes | JAMA | JAMA Network

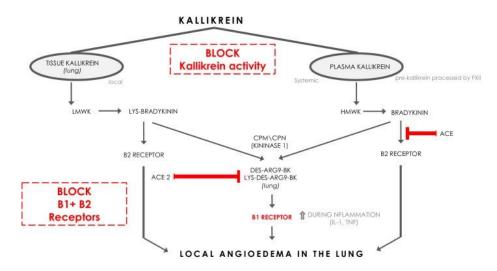
One reason for this is that blood vessels can dilate properly only if the endothelium is intact. In addition, the blood pressure lowering effect of supplemental arginine is brought about via bradykinin and inflammatory nitric oxide, when healthful nitric oxide is low. Bradykinin stimulates "rapid increase in l-arginine uptake" for des-Arginine9 bradykinin, which becomes inflammatory nitric oxide via BK1. Bradykinin and ATP stimulate L-arginine uptake and nitric oxide release in vascular endothelial cells - PubMed (nih.gov) This would explain another heart attack since inflammatory nitric oxide "is obligatory for local and systemic inflammatory activation and cardiac remodeling (with a heart attack)." https://pubmed.ncbi.nlm.nih.gov/28238121/ Another possible effect of the supplementary arginine is increasing the action of the arginine hormone called arginine vasopressin, or anti-diuretic hormone, which raises blood pressure by retaining water. Diuretics are often used to lower blood pressure, so perhaps excessive arginine could have excessive ADH effects.

The difference in how dietary arginine and arginine made in the body produce nitric oxide is so confusing that it's been labeled the "arginine paradox". The paradox is that, when someone is

healthy, taking arginine doesn't increase the steady-state, constitutive nitric oxide, which is supplied by arginine made in the body, which is what body builders look for when taking arginine. Yet, supplemental arginine does increase it in unhealthy people, which is why they did the study. However, it helps only on a short-term basis whereas, as shown in this longer study of 6 months, it also increases inflammatory nitric oxide via bradykinin.

BRADYKININ Inflammatory nitric oxide as caused by bradykinin offers an important clue regarding COVID-19. COVID-19 is particularly high in arginine, for the protein spikes contain multiple arginines, which enable it to enter cells. A very confusing thing about COVID-19, according to Anthony Fauci, was that a study from September 2020 found that hypertension was, by far, the most common comorbidity in hospitalized COVID-19 patients, almost double that of diabetes. <u>Abstract P135: Covid-19 And Hypertension: Pooled Analysis Of Observational Studies | Hypertension (ahajournals.org)</u> According to Fauci, just having high blood pressure shouldn't have increased risk for severe symptoms, like the "local lung angioedema" that causes acute respiratory distress syndrome (ARDS).

This may be explained, first, by the action of COVID-19 on bradykinin. The virus increases bradykinin by making its entry point, enzyme ACE2, dysfunctional, and ACE2 is needed to degrade bradykinin. ACE2 is also needed to block the bradykinin inflammatory receptor (BK1), which produces inflammatory nitric oxide. So, if someone already has elevated bradykinin, COVID-19 blocking ACE2 leads to low arterial blood pressure, constricted veins, and leaky capillaries in the lung, causing acute respiratory distress syndrome. Kallikrein-kinin blockade in patients with COVID-19 to prevent acute respiratory distress syndrome - PMC (nih.gov).



The most prescribed medications for high blood pressure, ACE-inhibitors, do just that-elevate bradykinin! So, the reason COVID-19 is a problem for people with high blood pressure may be that many are taking ACE-inhibitors. Role of bradykinin in the vasodilator effects of losartan and enalapril in patients with heart failure - PubMed (nih.gov) Their elevated bradykinin would be raised even more by COVID-19, as it blocks degradation of bradykinin by ACE2 and adds arginine via its

spikes, plus this allows the conversion of des-**Arginine** 9-bradykinin into inflammatory nitric oxide. As a result, lysine is recommended to prevent and treat COVID-19 symptoms. <u>Lysine</u> Reported to Halt Coronaviruses: An Interview with Bill Sardi - WholeFoods Magazine

CANCER

Methylation of lysine activates major cancer-fighter and "Guardian of the genome" P53. Gene therapy – From the LabLit short story series P53 blocks inflammatory nitric oxide and its mitochondrial and DNA damage. Regulation of p53 function by lysine methylation - PMC (nih.gov) Lysine in P53 also stabilizes DNA for correct reading, silences cancer genes (leukemia, AIDS, HPV-which changed to an arginine substitution), plus it repairs DNA, preventing development of cancer!

<u>Lysine methyltransferase G9a is required for de novo DNA methylation and the establishment, but not the maintenance, of proviral silencing | PNAS Histone methyltransferase - Wikipedia Papillomavirus and p53 | Nature</u>

Lysine is needed for ketogenesis as induced by carnitine and inhibiting HDAC, and ketogenesis fights cancer through "inhibition of cell proliferation, induction of cell differentiation or apoptosis, and induction or repression of gene expression." Inhibition of Histone Deacetylase
Activity by Butyrate | The Journal of Nutrition | Oxford Academic (oup.com)
https://www.frontiersin.org/articles/10.3389/fphar.2017.00869/full As the active site for NPC1, lysine is needed to activate as well as terminate autophagy (clears away dysfunctional cells, like cancer cells), another function of ketogenesis. NPC1 also regulates mTOR (needed for cell growth and DNA reading), which is critical as unregulated mTOR is found with cancer, Alzheimer's, autism, diabetes, obesity, heart disease, and premature death. mTOR also inhibits autophagy, shortening lifespan, and thus is the most important target in longevity research. But, as a growth factor, arginine induces mTOR! Arginine | C6H14N4O2 - PubChem (nih.gov)

Lysine marks cancer and other dysfunctional cells for destruction by binding to ubiquitin. Notably, autophagy needs to be regulated so it won't break down the body excessively, and another function of the lysine in ubiquitin is to terminate autophagy. Thus, without adequate lysine, autophagy is uncontrolled and causes atrophy and "many disease states." Ubiquitin-mediated regulation of autophagy - PMC (nih.gov) The name "ubiquitin" comes from its ubiquitous presence in the body, so this is another reason for "why always lysine?". This function of lysine is so important that faulty ubiquination is a "crucial" part of the development of "cancer, metabolic syndromes, neurodegenerative diseases, autoimmunity, inflammatory disorders, infection and muscle dystrophies". Ubiquitination in disease pathogenesis and treatment - PubMed (nih.gov) With many chemicals binding to lysine residues, limiting their availability, extra lysine is likely needed for these diseases. In addition, strong, stable collagen helps prevent pathogen entry into cells, that can cause cancer.

In stark contrast, polyamines from excessive dietary arginine feeds cancer cells and toxoplasma, increases IGF-1 (promotes cancer cell proliferation), plus "arginine enhances tumor growth".

Effects of l-arginine on growth hormone and insulin-like growth factor 1 - PMC (nih.gov) http://www.ncbi.nlm.nih.gov/pubmed/11061509 Most cancer cells can't reproduce without dietary arginine. Healthy cells are able to get the arginine they need for normal growth by converting arginine precursors like glutamine, the most abundant amino acid in the body, into arginine, but cancer cells aren't able to do this. As a result, arginine deprivation decreases inflammatory NO, decreases tumor growth factor IGF-1, decreases mTOR, and shrinks tumors. So, "arginine deprivation is a strategy for tumor reduction".

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8306961/ Cancers | Free Full-Text | Arginine Signaling and Cancer Metabolism (mdpi.com) In addition, nitrosamines are formed specifically from arginine, and these are strong carcinogens that may produce cancer in diverse organs and tissues including lung, brain, liver, kidney, bladder, stomach, esophagus, and nasal sinus.

L-arginine-dependent formation of N-nitrosamines by the cytosol of macrophages activated with lipopolysaccharide and interferon-gamma - PubMed (nih.gov)

METHYLATION AND ANTIOXIDANTS In the process of making ornithine from endogenous arginine, creatine is made for muscles. This process uses up 70% of the body's methyl groups. Methylation is extremely important, for it's needed to prevent cancer and many other functions:

- Correct reading of DNA, prevents cancer and birth defects
- Detoxification
- Repair, cell regeneration, anti-aging, prevents brain/muscle deterioration
- Lowers oxidative stress
- Cerebral blood flow
- Circadian rhythm: proper sleep
- Dopamine, serotonin
- Epinephrine: anti-histamine
- Norepinephrine: anti-depressant

Even though dietary arginine doesn't increase creatine, 9 grams of arginine per day was found to lower methyl groups, thus impairing vital methylation! This problem may relate to arginine's role in cancer. This dose also raised homocysteine, so it affected the homocysteine cycle, which generates methyl groups by recycling homocysteine. The homocysteine cycle is critical for detoxification, as it produces the powerful antioxidant glutathione, which is far more powerful and necessary than the highly praised antioxidants in nuts and chocolate. Yet, this cycle is often impaired, especially with 50% of Americans having the MTHFR gene variation. So, a high arginine diet may partly explain why vegans have high homocysteine (probably low methylation as well) and low glutathione. B-vitamin status and concentrations of homocysteine in Austrian omnivores, vegetarians and vegans - PubMed (nih.gov) [Alternative nutrition and glutathione levels] - PubMed (nih.gov) The researchers also noted that, "given the known adverse effects of homocysteine on endothelial function, L-arginine has the potential to paradoxically impair endothelial function." The Effect of L-Arginine and Creatine on Vascular Function and Homocysteine Metabolism - PMC (nih.gov)

In contrast, as shown with the study where arginine was first given to induce pancreatitis, lysine increased superoxide dismutase, catalase, and glutathione. Notably, glutathione recycles the antioxidant vitamin C, which is needed to detoxify peroxynitrite and form collagen. Furthermore, lysine is needed to activate MnSOD, the critical anti-oxidant of our mitochondria. Acetylation of MnSOD directs enzymatic activity responding to cellular nutrient status or oxidative stress - PMC (nih.gov) Another consequence of the high arginine but low lysine diet of vegetarians is that carnitine, critical for heart health, is deficient. Correlation of carnitine levels to methionine and lysine intake - PubMed (nih.gov) This may explain why vegetarians are more at risk for stroke, which is related to low carnitine. In contrast, lysine decreases risk for stroke. Lysine Uses, Benefits & Dosage - Drugs.com Herbal Database Lysine also forms glycine when it's converted to carnitine, and glycine plays major parts in the entire detoxification/homocysteine cycle, with glutathione as a major end product. Risks of ischaemic heart disease and stroke in meat eaters, fish eaters, and vegetarians over 18 years of follow-up: results from the prospective EPIC-Oxford study - PubMed (nih.gov)

MENTAL AND NEUROLOGICAL DISORDERS

Inflammatory nitric oxide is a major problem in the brain, where peroxynitrite causes brain damage, while healthful neuronal nitric oxide, made via lysine, is low. "NO is thought to be involved in neuroinflammation due to its free radical properties, which compromise cellular integrity and viability via **mitochondrial damage**."

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8771107/

https://pubmed.ncbi.nlm.nih.gov/15265275/ So, inflammatory nitric oxide is a major factor with mental illnesses and neurological disorders, such as seizures. One problem is that it prevents adequate blood flow, with its vital supply of oxygen, to the brain. Excess arginine is also converted into glutamate, and excessive glutamate is neurotoxic and pathogenic with mental and neurological disorders.

In contrast, lysine protects the brain and nervous system, for it prevents neuronal nitric oxide from "uncoupling" and becoming inflammatory by controlling arginine actions, and prevents seizures by a barbiturate-like action. https://pubmed.ncbi.nlm.nih.gov/8587651/ Notably, lysine, as acetyl CoA, is a component of the primary neurotransmitter of the normal, steady-state nervous system, acetylcholine. Acetylcholine induces the "in-the-flow" alpha state of the brain, needed for memory and learning, as well as proper vasodilation (relaxation for blood flow) in the circulatory system. This is seen with lysine's calming effects on people with anxiety who are low in lysine. In a study of people in Syria who ate mainly wheat, lysine fortification of flour reduced the cortisol response to stress and reduced chronic anxiety, and in a mouse study, lysine lowered anxiety and stress-induced diarrhea. Lysine fortification reduces anxiety and lessens stress in family ... High cortisol levels is a problem with adrenal fatigue, so lysine should help with that. www.pnas.org/doi/10.1073/pnas.2436556100 Along these lines, lysine regulates all the adrenal stress hormones, like adrenalin (epinephrine), which is an antihistamine. including aldosterone, which normalizes blood pressure.

https://pubmed.ncbi.nlm.nih.gov/28103616/ Lysine also controls opioid transit, as required for repair (this was identified in the retina).

AGININE VASOPRESSIN VS. OXYTOCIN Another arginine hormone, arginine vasopressin, stimulates release of cortisol. https://pubmed.ncbi.nlm.nih.gov/7684742/ This is probably because AVP stimulates the fear center of the brain-the amygdala. In contrast, oxytocin, which is the lysine counterpart to AVP, inhibits neurons in the amygdala, so it's calming. overview.of.cellular.electrophysiological.actions.of.vasopressin-ScienceDirect Oxytocin and AVP are the same structure, except that AVP has 2 additional amino acids, one of which is arginine. Males have more AVP receptors, and it's needed for male sexual arousal and long-term memory. It is interesting that the most commonly used drugs-caffeine, alcohol, and marijuana-inhibit AVP. Lithium, a mood elevator used to treat neurological disorders, paranoia, and addictions, also inhibits AVP. Thus, excessive AVP may cause a need for these drugs.

In addition, lysine is needed for calming neurotransmitter GABA, which is made from glutamate, and excess glutamate is neurotoxic. Thus, supplementation reduced chronic anxiety in a poor population in Ghana. Differential modulation of sodium- and chloride-dependent opioid peptide transport system by small nonopioid peptides and free amino acids - PubMed (nih.gov) Effect of lysine supplementation on health and morbidity in subjects belonging to poor peri-urban households in Accra, Ghana | The American Journal of Clinical Nutrition | Oxford Academic (oup.com) In addition, by maintaining proper levels of serotonin, lysine improves symptoms with schizophrenia. L-lysine as adjunctive treatment in patients with schizophrenia: a single-blinded, randomized, cross-over pilot study | BMC Medicine | Full Text (biomedcentral.com) Also, GABA is low with schizophrenia, while arginase activity is increased. Plus, the lysine enzyme OAT, which prevents production of polyamines by ODC, is deficient, so ODC is increased. As a result, polyamine production is increased with schizophrenia, as well as with mood disorders, anxiety, suicide, depression, and bipolar. Importantly, polyamines feed the brain parasite toxoplasma gondii, and toxoplasma has been linked to all of these disorders. Implication of the polyamine system in mental disorders - PMC (nih.gov)

Lysine is needed to activate myelin repair, and impaired myelin is found with mental and neurological disorders. So, when lysine was given to mice, it reduced MS symptoms and suppressed disease progression. https://mospace.umsystem.edu/xmlui/handle/10355/1565
<a href="mailto:Bromodomains: Translating the words of lysine acetylation into myelin injury and repair - PubMed (nih.gov) In contrast, there is "substantial" inflammatory nitric oxide with MS, and this blocks M2 macrophage debris clean-up (debris is a basic driver of autoimmune diseases). So, lysine's role in lowering inflammatory nitric oxide helped here as well.

Similarly, inflammatory nitric oxide is found with Parkinson's, ALS, autism, Asperger's, obsessive compulsive disorder, bipolar, schizophrenia, recklessness, suicide, traumatic brain injury, and Alzheimer's, and with diseases that can involve mental illness: headache, fibromyalgia, rheumatoid arthritis, obesity, type 1 and 2 diabetes, restless legs, and pellagra. Possible role of nitric oxide and adrenomedullin in bipolar affective disorder - PubMed (nih.gov) Nitric oxide pathways in Alzheimer's disease and other neurodegenerative dementias - PubMed (nih.gov)

Thus, an inflammatory nitric oxide blocker improved cortical thickness with traumatic brain injury, needed for memory, attention, speech, and learning. The role of L-arginine metabolism in neurocritical care patients - PMC (nih.gov)

SUMMARY

The great importance of lysine, combined with the problems of arginine, begs the question: are seeds a natural, healthy food for humans? The only mammals who eat seeds in the wild are small rodents who have a very different digestive system, for they have a cecum with extra gut bacteria to break down the seeds. Also, squirrels ferment their nuts in their cheeks, and by hiding them over the winter. Perhaps most important, birds are the other major consumers of seeds, and they have no ability to make arginine!-so arginine is an essential amino for them. So, perhaps it's best to leave the seeds to them, at least for the most part, while we make sure that we have a high lysine diet.

There has been a sea change in the American diet, from high-lysine seafood, meat soups and stews, sourdough bread, dairy products, beans, and roots, with seasonal high arginine nuts and berries, to a heavy emphasis on high arginine unfermented wheat, soybeans and peanuts, nuts, seeds, chocolate, berries, and added sugar. This new diet, along with widespread exposure to chemicals that bind to lysine, thus depleting it, and farm animals and fish that are fed cottonseed meal, has probably led to widespread lysine deficiency. Thus, our new diet is likely to have contributed in important ways to the development of the modern health problems that have plagued Americans since the early 1900's. However, this dire situation can be helped with a change for the better: back to a high lysine/low arginine traditional diet that is mainly meat and milk products from pastured animals, wild-caught seafood, a small amount of fermented lower arginine rye bread, low carb roots, and seasonal nuts and berries, along with careful avoidance of chemicals.

In addition, it might be a good idea to supplement with lysine, especially if you have been eating a high arginine diet, like I was, or if you have any of the disorders described in this article. It is always best to ask your healthcare provider for advice regarding L-lysine supplementation, especially with regards to dosage. According to experts at the University of Maryland Medical Center, the usual recommended dose for people aged 13 years and above is 12 milligrams (mg) per kilogram (kg) of body weight per day. For treating herpes infections, one may need a higher dosage, ranging from 3,000 - 9,000 mg, taken in divided doses, daily. To prevent recurrences, one may need to take 1,000 mg three times a day. Consult a physician for more information on proper dosage and duration of intake. Benefits of L-lysine & Ways to Avoid Its Deficiency | New Health Advisor (md-health.com)

Although I made some other changes to my diet as well, my experience of changing my high arginine diet to a high lysine diet, as well as supplementing lysine, shows the amazing power of this one amino acid. My disability seems like a long-ago dream, or, I should say, nightmare. At this point, I can only thank God that I was finally led to listen to the wisdom of my ancestors,

who, over many centuries, learned how to be strong, healthy, and happy-by eating a high lysine diet, and I hope that you're now inspired to try it for yourself!

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