LINUS PAULING INSTITUTE

OREGON STATE UNIVERSITY
RESEARCH NEWSLETTER

SPRING–SUMMER 2019

Free Public Lecture at the LPI Conference **LOOK INSIDE ►**

DIVING INTO DYSFUNCTION:

AN INTRODUCTION TO THE RESEARCH OF THE MAGNUSSON LABORATORY

by Kathy Magnusson, DVM, PhD

The Magnusson laboratory has been active on the OSU campus for the last 14 years. Originally hired in the College of Veterinary Medicine, Kathy Magnusson joined the Linus Pauling Institute in 2013. Currently, she is working to develop new cognitive tests for use in clinical studies in older adults.

Introduction

The brain changes as we age. I am interested in finding ways to prevent or repair some of these changes, especially age-related declines of learning and memory.

On the other hand, I am not as young as I used to be, so you could also say that I am hoping to figure out how to improve memory problems before I forget what I am researching!

A primary focus of my laboratory is discovering the molecular mechanisms underlying the changes that contribute to age-related memory decline. I focus on the changes that occur to a complex of brain-specific proteins known as the NMDA receptor – a brain protein important to memory formation.

Learning from NMDA

The NMDA receptor is a gated channel in neurons. It allows positively charged ions to enter the neuron when the amino acid glutamate binds to its surface. After the gate opens, the flood of ions sends a pulse through the brain cell.

The NMDA receptor is a focus of our work for two reasons: it is very important in the

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Oregon State University
Linus Pauling Institute

Richard van Breemen, PhD
Endowed Chair and
Director, Linus Pauling Institute

FROM THE DIRECTOR

In this issue of the Research Newsletter, the Linus Pauling Institute looks ahead to our 10th biennial conference, to be held August 14-16, 2019 on the Oregon State University campus.

One of the conference sessions will explore new approaches to the treatment of neurodegenerative conditions like Alzheimer's disease. Another session is dedicated to the role that oxidation/reduction reactions play in biology, especially in neurodegeneration, inflammation, and cancer. Lastly, we will discuss how nutrition and dietary supplements can help maintain cognitive resilience and prevent neurodegeneration.

Thus, it is only proper that in this issue we feature Dr. Kathy Magnusson's laboratory on the cover. Her work on campus for the last 14 years spans many aspects of neuroscience, and now her work in the LPI studies the effects of dietary supplements on cognitive function.

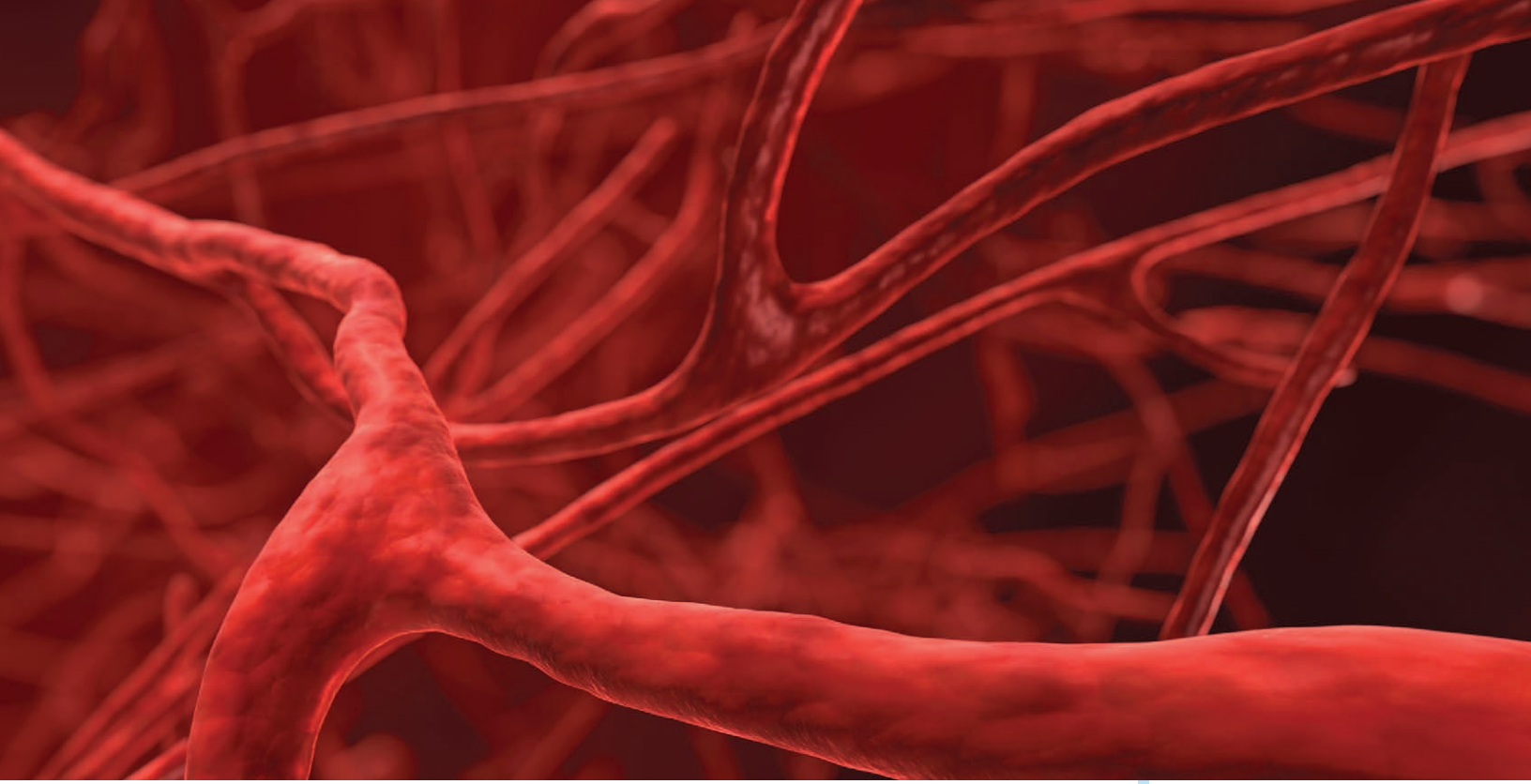
In my Fall/Winter 2018 column, I described how Linus Pauling contributed to passage of the Dietary Supplement Health and Education Act in 1994 (also known as DSHEA). Still law today, DSHEA ensures that dietary supplements like vitamins, minerals, and botanical supplements remain non-prescription and available over-the-counter to all consumers.

In recognition of the 25th anniversary of DSHEA, our upcoming conference will include a session concerning regulatory and research priorities for botanical dietary supplements. We will feature presentations by scientists from the National Institutes of Health, the Food and Drug Administration, and the dietary supplements industry. Sessions throughout the conference will describe the health benefits and mechanisms of action of many phytochemicals, as well as vitamins.

Our conference will close with a public session featuring Dr. Louis J. Ignarro, who shared the Nobel Prize in Physiology or Medicine in 1998. His presentation, "The Road to Stockholm – A Nobel Mission," will be free for all. We only ask that audience members register online to reserve their seat.

In his Nobel Prize winning research, Dr. Ignarro discovered that a molecule produced by the body called nitric oxide relaxes vascular smooth muscle. This amazing molecule can improve cardiovascular function, lowering blood pressure and inhibiting platelet aggregation. It also functions as a neurotransmitter mediating erectile function and is responsible for the biological actions of nitroglycerin and endothelium-derived relaxing factor.

Among his many achievements, Dr. Ignarro was elected to the National Academy of Sciences, the American Academy of Arts and Sciences, and the National Academy of Medicine. He was honored year after year as an outstanding teacher first while on the faculty of Tulane University and then at UCLA, where he is currently Professor Emeritus in the Department of Molecular and Medical Pharmacology.



Dr. Ignarro interacted with Dr. Pauling in the 1950s and 1960s. Their first meeting took place while Dr. Ignarro was attending high school in Brooklyn, NY. In his own words:

> *"I first met Linus Pauling in 1956, two years after his Nobel Prize in Chemistry. My high school chemistry teacher invited him to Long Beach High to assist in setting up a chemistry lab to complement the course lectures, and also to give a general experimental demonstration to the high school in the auditorium.*
>
> *Since my teacher knew of my passion for chemistry, I had the opportunity to work with Professor Pauling for many hours. There has never been any doubt in my mind that Linus Pauling was the most important motivating factor accounting for my success as a chemical pharmacologist."*

Dr. Ignarro's work showed that the body produces nitric oxide in order to control the constriction of blood vessels. The delivery of nitric oxide into the bloodstream can cause constricted arteries to relax, ultimately lowering blood pressure.

The conference is being held in conjunction with the Society for Redox Biology and Medicine, and I am grateful to Maria C. Franco of the OSU Department of Biochemistry and Biophysics who is representing the SfRBM in planning this event.

I would also like to thank the LPI conference committee for their diligence in organizing the conference: LPI principal investigators Maret Traber, Fred Stevens and Fritz Gombart, with LPI staff members Alex Michels, Dustin Helvie, and Caitlyn Reilley. Also I thank Jen Stotts and all of her hard-working team at OSU Conference Services.

Please consider coming to Corvallis in August. If you can attend the entire conference or just the public session, all of us at the LPI would be delighted to see you.

Sincerely,

Richard B. van Breemen

Continued from cover — **Diving into Dysfunction**

Dr. Magnusson is a principal investigator at the Linus Pauling Institute and is a professor in the College of Veterinary Medicine at OSU

formation of memories, and it shows problems binding to glutamate with increased age. In comparison to other glutamate receptors in the brain, the NDMA receptor shows more deficits with age. These changes affect both short- and long-term memory.

Observing biochemical changes in the NMDA receptor requires a detailed analysis of the protein, including how much of it is functional and expressed on the surface of a neuron. This is also the way we characterize other modifications present on the protein that might affect its function.

We use this information to devise interventions that may reverse brain aging. If successful, this would change or slow the modifications on the NMDA receptor and allow it to look and function more like it does in the brains of younger animals.

While a detailed analysis of the NMDA receptor is very valuable, it is only one piece of a puzzle that can help us improve cognitive function. What we need to do is link these biochemical changes to something functional.

In other words, how do we really know that any given change might affect memory?

More than just a Swim Test

Cognitive function tests for rodents are used to probe certain brain functions. For example, if you want to test the anxiety level in a laboratory animal, you can use a test that puts them in a light versus dark environment. Because rodents typically associate safety with darkness, the amount of time that they stay in a dark area can be associated with their anxiety level.

For memory tests, we take a different approach. Repeated trials to find food in an environment or to locate an object can test long-term memory. Once an animal has learned a particular location or task well enough, we can change something about the test and measure their **cognitive flexibility**. This adaptability to new situations tends to decline as the animal gets older.

Cognitive flexibility is defined as the ability to adjust and remember a change, or shift from thinking about one topic to another.

Another way to test long-term memory is novel object recognition, which takes advantage of the natural curiosity of mice. After a given time period to become familiar with an object, mice are less likely to investigate it – that is, assuming they remember it. Mice spend less time exploring an object that is familiar to them.

For different aspects of memory that involve spatial learning, our laboratory utilizes the Morris Water Maze. In short, this is swim test for mice. We put them in a round pool filled with water that contains a platform. In order for the animals to get out of the water (which they are very eager to do), they must swim to the platform.

The difficulty is that the platform is hidden just under the surface of the water. The water is made opaque, so they can't see the platform and swim toward it. When the animals are placed in the pool, they swim around until they find the platform. Every subsequent time that they are placed inside the pool, they will do the same thing: search until they find the platform.

To help the animals orient themselves in the round pool, objects or distinctive shapes are placed around the pool edge. If the animal finds the platform in a particular location, it will use the objects as landmarks to locate it faster on the next trial.

Once the mice learn that the objects tell them where the platform is, the faster the animal will swim directly to it. If the platform is removed, animals with a good memory will still search that area first before looking for the platform in other areas. Removing the platform helps us to see whether the animal knows where the platform is supposed to be and is not just swimming fast and running into it randomly.

We use this swim test extensively to link changes in the NMDA receptor to memory declines with age. We can identify some older mice that perform almost as well as younger animals, while others perform much worse. Older animals with good memories have distinctly different NMDA receptors than their poor-performing counterparts. This suggests they can compensate for the natural changes that occur with age.

Recently, we found more of a fatty acid called palmitate attached to NMDA receptors of aged animals. These palmitate deposits are associated with more memory problems and seems to be a phenomenon of the aging process. It does not appear that we can do much to reduce palmitate levels on these proteins, but maybe we can influence other ways the brain can adapt?

Bringing it Home

Although research in rodents is the foundation of much of the scientific work on memory, there is a big push to bring this work out of animals and into people. This process is known as translation – a complicated way of saying that we are trying to find ways for animal studies to be repeated in human volunteers.

To enhance the translation of our work, we have been developing a water maze for testing human subjects. Unlike the rodent test, this is not performed in a pool of water but in a virtual computer environment. Otherwise, this task is designed to be similar to the water maze task that we use to assess memory in mice.

Using this 'virtual water maze,' we find that young adults learn the test in a very similar pattern as young animals. Like the mice in the pool, the participants use the landmarks on the computer screen to navigate the environment. Over repeated tests, their time to find the hidden platform quickens.

However, older adults appear to learn much slower in water maze, even slower than the animal testing would predict. Why? Well, there are several possibilities. One is that older adults are not comfortable navigating a computerized environment while most young adults have been 'training' in this environment since they were children.

Another possibility is a motivation factor. Mice in a pool want to get out of the water as soon as possible. Navigating a computer environment means no reward for success, and no risks in failure.

However, we are able to divide participants into good performers and poor performers, just like we do for the mice. We can then monitor active brain regions that might be important to performance using equipment such as an **fMRI**.

We believe that using a virtual test will enhance our ability to transition from animals to humans. We are currently using the virtual water maze in a study of cognitive function in veterans from different war eras.

The Gut-Brain Connection

Our virtual water maze is a very effective tool for measuring the effects of an intervention. One of our ongoing studies, in partnership with Dr. Tory Hagen, looks at how multivitamin supplements might alter cognitive function in older men.

We also have experience examining the roles that diet and gut microbiota play in cognitive abilities. Our recent animal studies show that eating a high-sucrose diet can cause specific learning deficits. Also, animals fed either a high-fat or a high-sucrose diet have trouble with cognitive flexibility.

The composition of the gut microbiota seems to play a big role here – animals that show the most changes in gut bacteria after switching to these diet tend to have more cognitive problems. We are pursuing evidence of whether these cognitive deficits are due to diet alone or to the microbiota, but either scenario provides some exciting opportunities for intervention.

You will hear more from my laboratory on this topic soon. We are very excited to explore new avenues of cognitive testing at the LPI, and cannot wait to share what we have learned about the influence that gut bacteria have on anxiety.

fMRI refers to Functional Magnetic Resonance Imaging, a way to monitor brain activity in real time.

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VITAMIN C TO THE RESCUE:

STEMMING ANTIOXIDANT DEPLETION IN METABOLIC SYNDROME

Gut dysbiosis in metabolic syndrome reduces vitamin E availability. Dr. Maret Traber and her colleagues think that healing the gut might just require a little extra vitamin C.

Dr. Traber is the Ava Helen Pauling Endowed Professor at the Linus Pauling Institute and a professor in the College of Public Health and Human Sciences at OSU.

It is no secret that a diet high in saturated fat and processed food and low in fruit and vegetables is not doing the body any favors. Not only is such a diet low in many vitamins and minerals, but it can also lead to a host of problems with your gut microbiome and can promote intestinal dysbiosis (see p.7).

Dr. Maret Traber highlights antioxidant depletion as one of the symptoms of the dysbiosis seen in metabolic syndrome. Specifically, Traber and her colleagues, Drs. Garry Buettner and Richard Bruno, have been focusing on how vitamin C and vitamin E are affected by this condition.

In a recently published review in the journal *Redox Biology*, they suggest that changes in the gut microbiome and increases in inflammation seen with metabolic syndrome can easily result in vitamin C depletion, and this can lead to vitamin E depletion.

Antioxidants like vitamins C and E are the first line of defense against oxidative stress brought on by free radicals – unstable molecules that can damage cells. Vitamin E is particularly good at stopping the oxidation of fats, especially those that reside in the membrane of cells.

A limitation to this protection is that once vitamin E is oxidized, it can no longer participate in antioxidant defense. Since vitamin C can regenerate the antioxidant capacity of vitamin E, it is only natural to think about the combining the two antioxidants.

"Vitamin C normally helps support vitamin E activity," Traber explains. "On the other hand, if you do not have enough vitamin C, vitamin E can be destroyed. This is the start of a process that leads to the loss of both antioxidants."

One particularly insidious source of free radicals in the body is our own immune system. Activated immune cells create a host of free radicals to fight off invaders. Although helpful to stop infections, problems arise when the immune system goes out of control.

Also, immune cells go on high alert when pieces of bacterial cell walls enter into the bloodstream. This response is a hallmark of metabolic syndrome, as well as other diseases that involve both an imbalance in the gut microbiome and a loss of integrity of the intestinal wall.

"Essentially, white blood cells are scrubbing our bodies with bleach because fragments of bacteria cells are fooling them. They are responding as if there was an ongoing bacterial invasion when none exists," Traber said. "Now, instead of destroying bacteria, this bleach destroys vitamin C, eroding the body's own protective mechanisms."

The overactive immune system causes inflammation that paves the road for the production of more free radicals. Without an intervention, this process keeps repeating.

Is vitamin E a solution to the problem? Only in part. If you could increase the amount of vitamin E in the body, it would be better equipped to fight off lipid peroxidation.

"We have performed studies measuring vitamin E in people with metabolic syndrome, and they showed some interesting results," Dr. Traber explains. "In short, we found when we gave vitamin E to people who were healthy and to those with metabolic syndrome, the healthy people had higher vitamin E in the bloodstream. We think this is because of low vitamin C status in people with metabolic syndrome."

Without vitamin C, adding more vitamin E becomes very inefficient. Restoring vitamin C levels should be the priority.

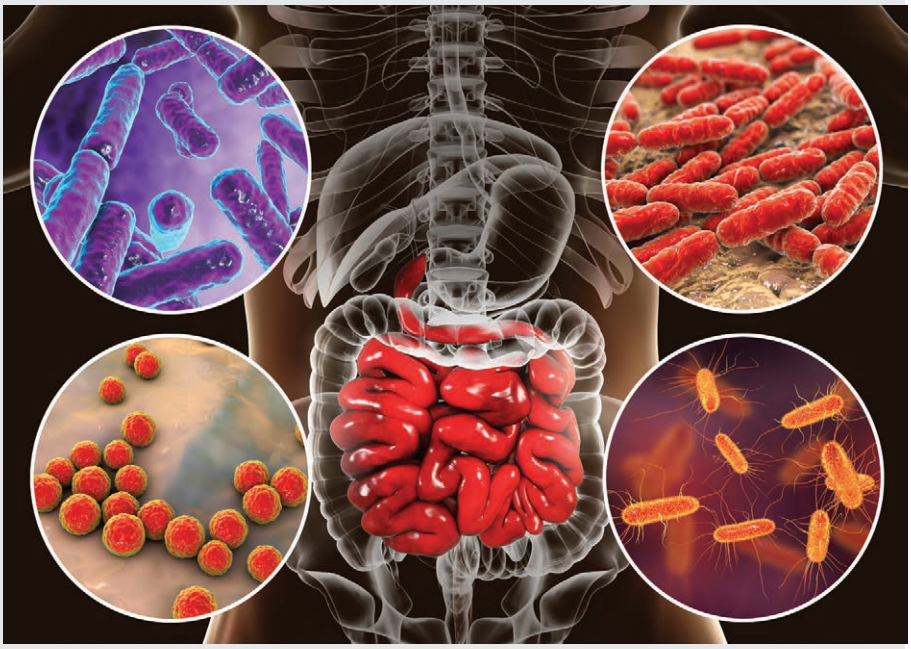
The benefits of maintaining a high vitamin C status are multifold. Besides being a versatile antioxidant, vitamin C can lower inflammation and support 'leaky' cells in the gut. It may even alter growth of certain gut bacteria.

Gut Microbiota and Your Health

The human gastrointestinal tract has an abundance of microorganisms from the environment. The collection of different single cell organisms colonizing the gastrointestinal tract is termed the 'gut microbiota.'

The relationship between these microorganisms and our health can get quite complicated. Although generally beneficial, there is potential for dysfunction as a result of an altered microbial composition – known as **dysbiosis**.

As researchers explore the links between the microbiota and our health, it can become apparent that a large number of diseases have links to dysbiosis. Therefore, correcting or preventing dysbiosis is of particular interest in health research.



Researchers at the Linus Pauling Institute have explored gut microbiota in several studies over the past few years:

Dr. Kathy Magnusson explores the effects of dysbiosis on cognitive function in mice (see Magnusson article, *cover*).

Dr. Emily Ho studies the effects of zinc and aging on the gut microbiome in mice and how they are related to inflammation.

Studies by **Dr. Adrian Gombart** and **Dr. Fred Stevens** have focused on improving gut health with derivatives of xanthohumol (see our Fall/Winter 2018 Research Newsletter).

Traber and her colleagues believe there is sufficient evidence that the government's **recommended intake levels** for vitamin C (75-90 mg for women and men, respectively) might not be enough. She supports the Linus Pauling Institute recommendation that every adult should consume 400 mg of vitamin C every day.

Yet, adding more vitamin C is not a miracle cure. Traber and her colleagues have found that when people with metabolic syndrome consume vitamin C, their plasma concentrations of the vitamin remain low. Something is happening to the vitamin, and Traber thinks that is because the dysbiosis and rampant inflammation is not being properly addressed.

The ideal intervention for metabolic syndrome encompasses a complete overhaul of dietary habits.

"Ultimately, what these findings really say is: Eat your fruit and vegetables," Traber said "Five to ten servings a day will get you the fiber and antioxidants you need to restore beneficial bacteria, protect your gut, and ultimately increase vitamin C and vitamin E status in the body."

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Traber et al. *Redox Biology* **21 (2019)** doi: 10.1016/j.redox.2018.101091

Traber et al. *American Journal of Clinical Nutrition* **105 (2017)** doi: 10.3945/ajcn.116.138495

A TRUSTED RESOURCE FOR NUTRITION INFORMATION

The Linus Pauling Institute is home to one of the premier databases of evidence-based information on nutrients, phytochemicals, and other dietary factors. The Micronutrient Information Center website (lpi.oregonstate.edu/mic) has been an integral part of our communication efforts since its debut nearly 20 years ago.

Overview

The Micronutrient Information Center is an open-access, online repository of information designed to explain the roles of vitamins, minerals, and other dietary factors in the body, as well as the available evidence of their health effects.

Accessed by people from all over the world, it has been a trusted source of nutrition information for hundreds of thousands of people every year.

If you have not visited the Micronutrient Information Center website before, this article will serve as a primer on the available content. If you are already familiar with the database, you can skip ahead to page 9 to learn about our recent updates and our new developments.

Going In Depth

The bulk of the content on the Micronutrient Information Center is found under the **Articles** heading. This is where you will find in-depth articles on various nutrients and dietary factors, including food and beverages.

Written by PhD nutrition scientists, each article summarizes the current state of the scientific literature on the topic. In general, the articles are broken down into an overview of function, evidence for its role in disease prevention and treatment, typical food sources, and intake recommendations. Other information, such as toxicity and drug-nutrient interactions, is also included.

Not surprisingly, the articles on vitamins and minerals are the most popular on our site. However, you can also find information

about other dietary factors that contribute to health maintenance. In particular, the **Dietary Factors** section contains detailed information on several phytochemicals, i.e., biologically active, non-nutrient compounds synthesized by plants.

The section on **Food and Beverages** has articles on several foods and drinks that have purported health benefits, including cruciferous vegetables, nuts, and tea. A general overview on glycemic index and glycemic load can be found in this section, providing information to help people understand how carbohydrates influence blood sugar.

A Focus on Health & Disease

A fairly recent addition to the Micronutrient Information Center website is the **Health & Disease** section. Instead of looking up pages for each vitamin or mineral, this section places the relevant information on a health topic in one convenient location. Several health and disease conditions are already available, including pages on Alzheimer's disease, bone health, immunity, pregnancy, heart attack, and stroke, with more planned for the future.

With user-friendly infographics and easy-to-read summaries, any dedicated health seeker can quickly access information on nutrients and dietary factors related to a specific health condition.

From the Experts

Because human studies form the core of the information on our website, the Micronutrient Information Center provides information that informs healthy dietary and supplement choices.

The content found in our articles is derived from the published scientific literature, representing an independent view on the subject. Importantly, each article is reviewed by an expert in the field to ensure its accuracy and scientific validity.

If you are unable to access the Micronutrient Information Center website, some of the content is available as two hardbound books published by Thieme. If you are interested in purchasing either book, please contact the Linus Pauling Institute.

The Newest Additions

Supported by an "Independent Grant for Learning & Change" from Pfizer, scientists at the Micronutrient Information Center developed articles and companion online courses that are now available. These classes are geared toward healthcare professionals but available to anyone interested in the topic.

The first course, "**Meeting Micronutrient Needs**," has been accredited by the Commission on Dietetic Registration.

http://bit.ly/MicronutrientNeeds

The second course, "**Micronutrients and Bone Health**" is in the process of accreditation and should be available soon.

http://bit.ly/MICBoneHealth

Articles from the Micronutrient Information Center have now been translated into two other languages: Spanish and Japanese. This content is hosted on companion sites.

Articles recently updated on the site:

- **Lipoic Acid**, with expanded content on diabetes and a new section on weight management.
- **Magnesium**, with updated content on disease prevention and disease treatment.
- **Potassium**, with new intake recommendations and expanded content on stroke, osteoporosis, and hypertension.
- **Zinc**, with new content on disease prevention and disease treatment.

If you have a question about one of our articles, please email us at: **lpi.mic@oregonstate.edu**.

Support Us

The Micronutrient Information Center has always been freely available and will never contain ads – generous donations to the Linus Pauling Institute support its development and maintenance.

With more than a million visitors every year from around the globe, it is one of the most frequently visited websites at Oregon State University.

To support this program, contact the OSU Foundation and make a gift to the LPI's Outreach Education Fund.

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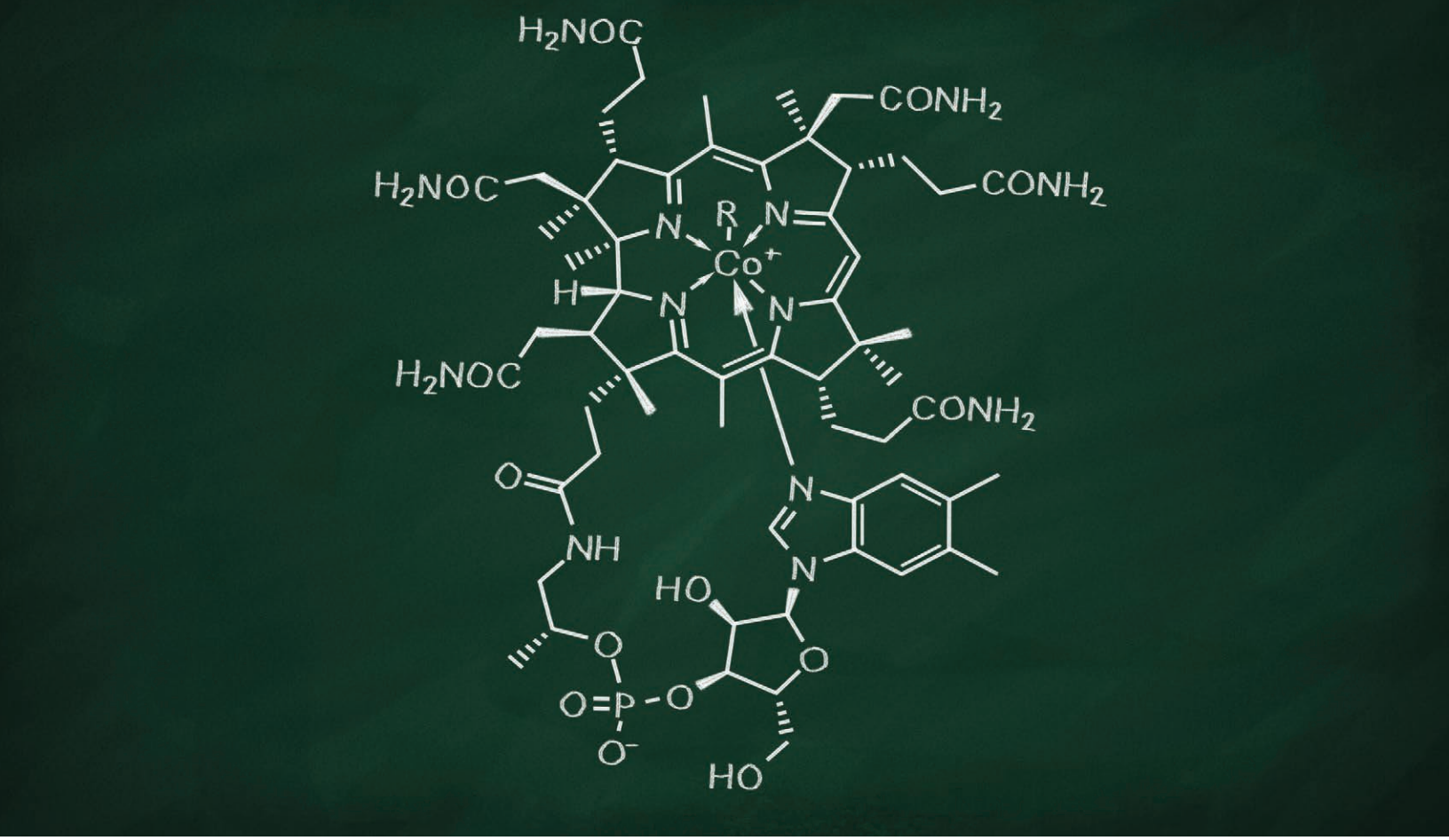

FREQUENTLY ASKED QUESTIONS ABOUT... VITAMIN B_{12}

The Linus Pauling Institute receives many questions from all over the world about micronutrients and dietary supplements. Here, we summarize some common questions about vitamin B_{12}.

What is vitamin B_{12}?

Vitamin B_{12} is known as cobalamin. It is the largest vitamin molecule and also the only vitamin that contains the element cobalt. Methylcobalamin and adenosylcobalamin are the two forms of "active" vitamin B_{12} used by the body.

Like all vitamins, the body is unable to make vitamin B_{12}. Synthesized only by bacteria, this vitamin is prevalent in animal products, including meats, fish, shellfish, dairy products, and eggs, and absent in plant-based foods.

What does vitamin B_{12} do?

Like all B vitamins, vitamin B_{12} functions as an enzyme cofactor in the body. It is used as a cofactor for methionine synthase — an enzyme that uses B_{12}, folate, and homocysteine to produce the amino acid methionine.

B_{12} is also used by methylmalonyl-CoA mutase, an enzyme that converts breakdown products of certain amino acids, cholesterol, and some fatty acids into usable fuel for the citric acid cycle in mitochondria. Without this enzyme activity, these breakdown products cause neurological damage that could be irreversible.

Sublingual forms of supplemental B_{12} are absorbed in a passive fashion. These can help those with inadequate vitamin B_{12} absorption in the intestine.

How is vitamin B_{12} absorbed?

Vitamin B_{12} absorption can occur in two different ways.

The first method is assisted transport, with the transfer of the B_{12} molecule to different carrier proteins in the digestive tract to ensure its stability. In this fashion, B_{12} is ultimately absorbed in the small intestine. If the body does not produce these carriers, very little vitamin B_{12} is absorbed.

There is an unassisted transport mechanism for this vitamin as well. In this mechanism, B_{12} moves in the spaces between cells in our digestive tract. This form of transport is very **inefficient**, with only about 1% of a given dose of B_{12} being absorbed.

What are the symptoms of B_{12} deficiency?

Vitamin B_{12} deficiency is characterized by a specific type of anemia called **megaloblastic anemia**. It can cause fatigue, weakness, constipation, loss of appetite, and weight loss. Numbness and tingling in the hands and feet, depression, confusion, or poor memory can also occur.

Symptoms of B_{12} deficiency can take decades to develop, and can usually only be diagnosed by a medical professional.

Who is at risk for B_{12} deficiency?

Vegans: Diets devoid of animal products will result in B_{12} deficiency. Vegans need to eat fortified food or use supplements to maintain their B_{12} levels.

Stomach acid blockers: Because adequate stomach acid is necessary to release vitamin B_{12} from the proteins to which it is bound, some types of **stomach acid blockers** can reduce vitamin B_{12} absorption from food.

Stomach inflammation: Autoimmune or inflammatory conditions of the stomach wall can degrade the proteins that aid vitamin B_{12} absorption, or stop their production entirely. People with these conditions often have low B_{12} status.

Older adults: A combination of chronic stomach inflammation and reduced stomach acid – which is more common in older adults – can reduce the absorption of vitamin B_{12} from food.

What are different forms of vitamin B_{12} supplements?

Vitamin B_{12} can be found in different supplemental forms, but each form of the vitamin (also called vitamers) can be converted to active B_{12} after absorption. The derivatives commonly found in these products are adenosylcobalamin, methylcobalamin, hydroxycobalamin, and cyanocobalamin.

Despite claims of better absorption, enhanced bioavailability, or lack of side effects, no differences in these forms of B_{12} have been observed in scientific studies. Sublingual forms of B_{12} may be helpful for those with absorption issues.

What are the recommendations for vitamin B_{12}?

The Recommended Dietary Allowance for vitamin B_{12} is 2.4 micrograms per day (µg/day) for adolescents and adults. It is slightly higher for women who are pregnant (2.6 µg/day) or breastfeeding (2.8 µg/day).

Because of the increased risk of malabsorption by adults over 50 years of age, they should get most of their B_{12} from fortified food or supplements. The Linus Pauling Institute recommends adults older than 50 years take 100 to 400 µg/day of supplemental vitamin B_{12}. Others may also have difficulty absorbing vitamin B_{12} from food, but determining this requires an evaluation of vitamin B_{12} status by a medical practitioner.

Vitamin B_{12} is present only in foods of animal origin, including dairy products and eggs. Thus, people following a vegan diet need to consume vitamin B_{12}-fortified food or use supplements to prevent B_{12} deficiency.

No toxic or adverse effects have been associated with large intakes of vitamin B_{12} from food or supplements in healthy people.

What is the latest research on vitamin B_{12}?

A recent study in the journal *Gerontology* showed that elevated blood concentrations of vitamin B_{12} were associated with increased risk of mortality in people 85 years or older. This garnered some attention from the media with the idea that B_{12} supplements could be harmful.

However, the authors of this study noted that taking B_{12} supplements was not a factor in this association, as less than 5% of people with high plasma vitamin B_{12} levels also took dietary supplements. Therefore, the idea that taking vitamin B_{12} supplements leads to death is quite misleading, to say the least.

What if I have more questions about vitamin B_{12}?

The Linus Pauling Institute has scientifically accurate information on vitamin B_{12} **on our website**.

As always, you can email your specific inquiries to **lpi.mic@oregonstate.edu**.

Linus Pauling's mother, Belle Pauling, suffered from pernicious anemia, one type of megaloblastic anemia caused by B_{12} deficiency.

Proton-pump inhibitors and H2-receptor blockers are two classes of stomach acid blockers associated with lower B_{12} absorption.

A quick link to the vitamin B_{12} page on the Micronutrient Information Center:

http://bit.ly/MIC-B12

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You start by transferring cash, stocks, real estate, or other property to fund the life-income gift. In return, you receive an income stream for the number of years that you choose. These payments to you (or another designee) can begin immediately or be deferred to a future date, such as a savings for your retirement.

For a personalized confidential illustration of how a life-income gift may work for you, please contact Andrew Norwood at the OSU Foundation: (503) 936-0086.

LPI STUDENTS

The Linus Pauling Institute provides financial support to a number of graduate students and postdoctoral researchers. This often comes in the form of fellowships, made possible by donations or endowments by generous LPI donors.

This year, the Institute selected three graduate students as recipients of new fellowships. Each of these fellowships is named for the generous donors that make student research opportunities possible.

For 2019, the following awardees were named: **John Bouranis** (Caron and Donald Reed Fellowship), **Emily Rue** (Balz Frei Fellowship), and **Isabelle Logan** (George and Audrey Varseveld Fellowship).

Each graduate student fellowship furthers our mission to train future scientists.

If you are interested in contributing to student fellowships, please contact the Linus Pauling Institute or the OSU Foundation.

John Bouranis - Public Health and Human Sciences

Ho Laboratory — The Caron and Donald Reed Fellowship

Cruciferous vegetables are a rich source of many essential micronutrients, such as vitamins E and K, but also a host of phytochemicals. Many of these phytochemicals act as antioxidants and modulate the gut microbiome, helping to prevent the onset of disease.

I have been working on biomarker discovery – finding ways to quantify the consumption of cruciferous vegetables. Ultimately, our hope is that more accurate, consistent measurements of dietary cruciferous vegetables will help elucidate the role they play in diseases like cancer.

We are also looking at the effects of zinc on the immune system and the gut microbiome. With the help of the LPI Core Laboratories, I am looking at short fatty acids in fecal samples – these fats act as a bridge between the gut microbiome and signals to the immune system. These molecules may be important in determining how age and diet influence human health.

Emily Rue - Pharmaceutical Sciences

van Breemen Laboratory — The Balz Frei Fellowship

Procyanidins, compounds known for their antioxidant activities, can be found in cranberries, cocoa, cinnamon, grape skins, and many more plants. Chemically, procyanidins are polymers of smaller flavonoids arranged in different ways. Antioxidant and therapeutic properties of procyanidins have made them attractive for many different research studies.

To expedite research on these compounds, I am working to identify and characterize procyanidins in plant extracts faster and more efficiently than ever before. Using a technique called positive ion electrospray ion mobility-mass spectrometry, we can separate and characterize these molecules in milliseconds, using only a fraction of the product that traditional methods use.

I have used this technique to characterize procyanidins in cranberries, cocoa, cinnamon, crab apples, and peanuts. We hope that the structural characteristics we identify in these procyanidins will help others better understand their therapeutic effects.

Isabelle Logan - George and Audrey Varseveld Fellowship

Isabelle is a PhD Student in Biochemistry and Biophysics, working with Dr. Adrian Gombart. Her work focuses on elucidating the roles of xanthohumol and its derivatives, especially in gut health and cancer. Isabelle was featured in our **Spring/Summer 2018 Research Newsletter**.

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