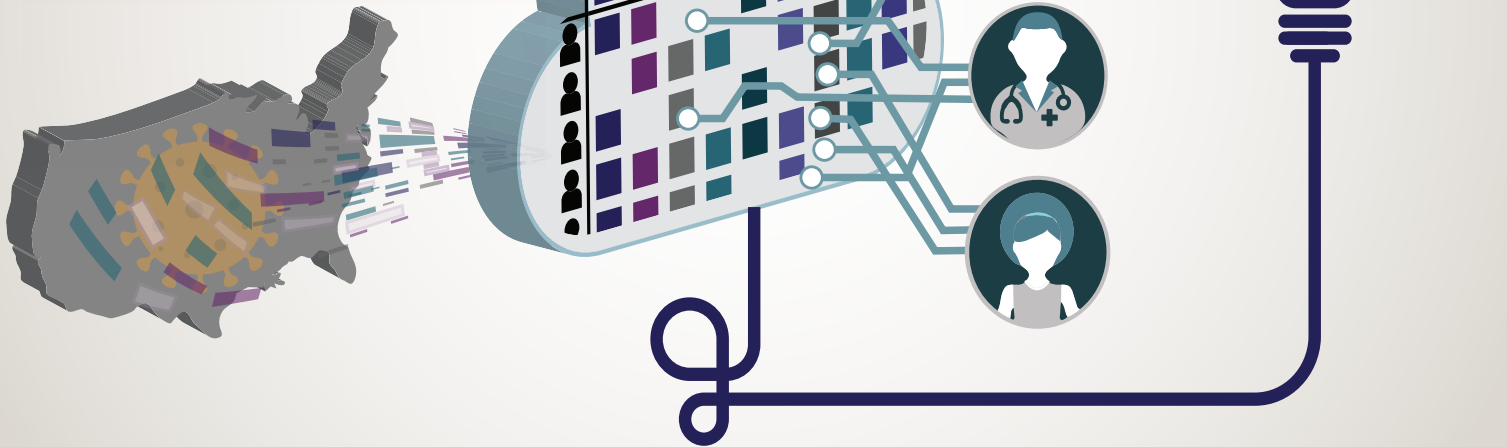


LINUS PAULING INSTITUTE

OREGON STATE UNIVERSITY
RESEARCH NEWSLETTER

SPECIAL EDITION 2020



Nutrients for the immune system **LOOK INSIDE** ▶

ACCESS GRANTED

Fighting COVID-19 with Big Data

As US doctors fight COVID-19 throughout the nation, an enormous amount of useful data is being generated. Because of the emergent nature of this pandemic, strategies to fight COVID-19 quickly evolve, and valuable information from patient records is scattered across the country.

How can researchers find patterns and clues for treatment options in such a widespread, disparate data stream?

Enter the **National COVID Cohort Collaborative**, also known as the **N3C**.

The N3C is a nationwide collaboration of clinicians, informaticians, and other biomedical researchers. The collaborative is tasked with two goals: collect COVID-19-related health information into a centralized data repository and create secure analytical tools to process that data.

The N3C is spearheaded by **Melissa Haendel, PhD**, principal investigator and Director of Translational Data Science at the Linus Pauling Institute. To propel this initiative, Dr. Haendel has brought together more than 60 clinical centers with the resources of the National Institutes of Health.

Supported in part by Oregon State University and the Oregon Clinical and Translational Research Institute at Oregon Health & Science University, the N3C will build, maintain, and regulate a new, secure database housing electronic health records from COVID-19 patients.

Putting the nation's health data together into one place is not as easy as it sounds. First of all, healthcare providers across the country use different record systems with no standard data format.

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Oregon State University
Linus Pauling Institute

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

FROM THE DIRECTOR

This special issue of the LPI Research Newsletter is focused on our ongoing efforts surrounding the COVID-19 pandemic. This issue features Dr. Melissa Haendel's work to help establish a first-of-its-kind nationwide database of COVID-19 patient information ([see front cover](#)). Also see our overview of what we know about IV vitamin C use in treating COVID-19 ([page 4](#)).

My research group is also joining the effort against the pandemic. We are using our patented affinity selection technology to discover natural compounds that can prevent COVID-19. Our approach capitalizes on the sensitivity, speed, and selectivity of mass spectrometry to identify specific compounds in complex mixtures (like botanical supplements) that can interact with therapeutic targets, such as viral proteins.

If our search is successful, we hope to be able to use plant-derived products in hand sanitizers, surface cleaning products, and even dietary supplements to prevent the SARS-CoV-2 virus from infecting human cells.

Despite the limitations that the global pandemic has placed on our lives, LPI researchers are still hard at work on our usual research projects.

My group recently reported the results of a clinical trial on hops supplements. We show that women using hops to control menopausal hot flashes may not have to worry about harmful drug interactions.

In addition, Dr. Adrian "Fritz" Gombart recently published a highly cited review addressing how supplements can maintain a well-functioning immune system ([see page 6](#)).

For references, see the sidebar or the LPI website. More articles will be published soon.

Thank you for reading this special edition of our newsletter. You will be hearing from us again very soon.

Please stay safe and healthy,

Richard B. van Breemen

References

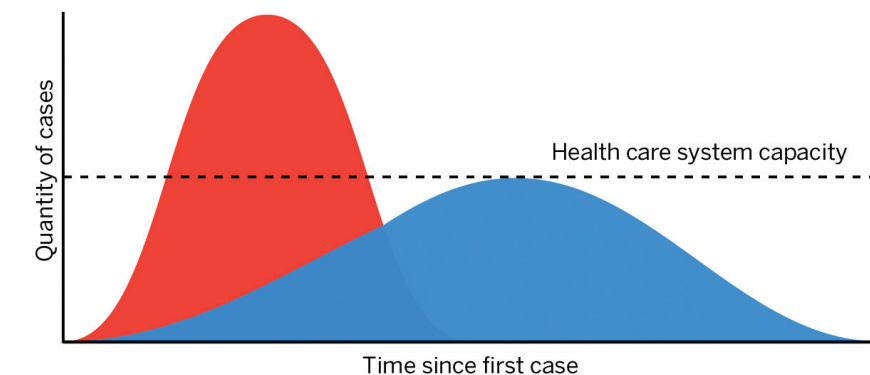
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FLATTENING THE CURVE

Julie McMurry, MPH, is part of Dr. Melissa Haendel's group at the LPI, has training in communicable diseases.

Early in this pandemic, McMurry knew it was important to act quickly and gather verifiable, accurate information on COVID-19.



This has now taken the form of a website: [FlattenTheCurve.com](https://www.flattenthecurve.com)

More than just a collection of scientifically accurate information, it is a centralized hub for proven COVID-19 strategies with a simple message: You can do something to stop this pandemic.

There is more online than we can summarize here, and the information is updated frequently. Explore the website to learn about COVID-19 and what you can do to help.

Julie McMurry, MPH, is an Assistant Professor of Practice at OSU's College of Public Health and Human Sciences

Continued from front page

“In the United States, there is no universal system for our healthcare data,” explains Haendel. “So you need to start by converting data into a common system. We have constructed a process for collecting electronic health records from many different institutions and storing them in the same format.”

The N3C takes data from disparate systems and standardizes them to a common architecture. In a process Haendel refers to as “harmonizing the data,” inconsistencies across health data structures are eliminated.

In effect, this harmonization translates the data from large hospitals and a variety of small clinics into the same language. Data consolidation opens up participation to a large variety of individual contributors, allowing all to join this nationwide initiative.

“One of the most important aspects of the N3C is that the data sources and methods are all fully reproducible. This allows greater transparency, invites community review, and increases the validity of the analyses the N3C facilitates.”

—Melissa Haendel, PhD

One advantage of this common framework is to facilitate the use of computer-based tools, such as machine learning and artificial intelligence. These types of analytical tools can quickly sift through the data to answer important questions.

“Machine learning algorithms can do things like reveal candidate drugs that reduce the severity of COVID-19 symptoms or build predictive analytics in assisting clinical care decisions,” Haendel explains.



National COVID Cohort Collaborative

Throughout this process, all the protected health information of COVID-19 patients remains safe. Only the vital pieces of the data, such as the progression of the disease or the effect of antivirals or other therapies, will be available to participating institutions with no risk of revealing patient identities.

Data for the N3C will be gathered from as much of America’s diverse populations as possible. This is more important than it might sound. Since the United States is comprised of people from many different ethnic and socioeconomic backgrounds, the N3C has the power to represent the health of many people from minority and disadvantaged communities.

The more clinics and hospitals that participate, the more it will be a resource for everyone in our country.

Several large hospitals are already uploading data to the N3C, but more clinical partners are **always needed**.

“It’s just unfortunate that it took a global pandemic to spur us into action,” Haendel continues, “This unique data system will be invaluable to researchers and clinicians.”

Ultimately, the N3C will be used to predict patient responses to antiviral or anti-inflammatory therapies, identify potential new treatments, and find other clinical tests that can inform decision making.

Because of its strong foundation, the N3C’s value against COVID-19 will grow in the weeks and months to come. 🌐

For more information on the N3C or how you can request access to data, go to:
<https://covid.cd2h.org>

Clinicians who are interested in contributing data or participating in this singular effort should send an email to:
data2health@gmail.com

IS INTRAVENOUS VITAMIN C EFFECTIVE AGAINST COVID-19?

A Review of the Theories and the Evidence

Every day, scientists at the LPI answer your questions about the use of IV vitamin C in the treatment of COVID-19.

We provide some in-depth information about this potential therapy here, but a summary is also on our website at: bit.ly/IV-VitaminC

Doctors on the front lines of the COVID-19 pandemic are using **intravenous (IV) vitamin C** (also known as ascorbic acid) to help people suffering from this disease.

As many LPI supporters know, IV vitamin C therapy is nothing new. Drs. Linus Pauling and Ewan Cameron used it to treat cancer patients nearly fifty years ago. Today, IV vitamin C is used against cancer, sepsis, infections, and other conditions.

Vitamin C plays an important role in the immune system (see pages 6-7), but IV vitamin C can do things that oral vitamin C supplements cannot.

To help you navigate this topic, we are providing an evidence-based primer on IV vitamin C and how it might work against serious infectious diseases like COVID-19.

Why use IV vitamin C?

Researchers and clinicians have experimented with IV vitamin C against various forms of infectious disease and cancer for nearly a century. However, clinical data using this approach have shown mixed results.

IV administration sends large doses of vitamin C directly into the bloodstream, bypassing the stomach and intestines. This approach often results in blood vitamin C levels in the millimolar (10^{-3} moles/L) range. By comparison, blood vitamin C levels only reach the high micromolar (from 10^{-5} to 10^{-4} moles/L) range after taking oral vitamin C supplements.

In other words, after IV administration, blood vitamin C levels are about 10 to 100 times higher than with supplements.

Such high concentrations allow IV vitamin C to have unique effects in the body. Since blood levels of vitamin C rise immediately, it can be an important tool for clinicians to use in emergency situations.

How might IV vitamin C work in COVID-19?

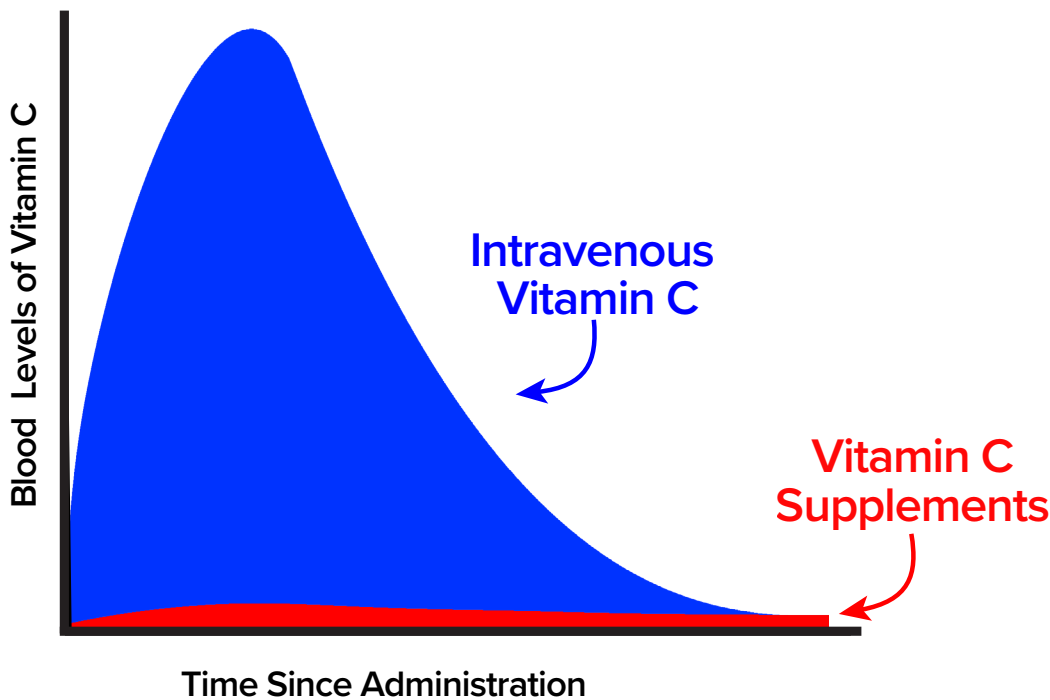
Because there are limited peer-reviewed data of IV vitamin C use against viral infections, we must rely on results from previous trials of other inflammatory conditions like sepsis.

Blood vitamin C levels in the millimolar range may create superoxide and hydrogen peroxide. In theory, these reactive oxygen species can inactivate viruses and destroy bacteria. While cells in our body have defenses against these reactive molecules, these pathogens do not.

Alternatively, IV vitamin C could dampen the harmful effects of an overactive immune system. A wave of inflammation and harmful oxidative reactions precedes the respiratory complications seen in severe COVID-19 patients. Early intervention is very important.

Excess inflammation could lead to lower vitamin C concentrations in the blood. COVID-19 patients can also have low levels of interferon, an antiviral cytokine. Could IV vitamin C boost interferon production and allow the body to mount an effective defense against the virus? It is one of many theories.





Blood Concentrations are Key

While vitamin C supplements can provide vital support to the immune system, oral supplementation cannot match the blood concentrations reached with IV administration.

It is still important to regularly take supplements and eat foods rich in vitamin C. This will maximize blood vitamin C levels in the long term.

IV vitamin C should only be used in a medical setting by trained clinicians who understand the safety issues involved.

How effective is IV vitamin C in treating COVID-19?

We simply do not know. There are currently **no published data** of IV vitamin C in the treatment of COVID-19.

Despite the emergence of SARS and MERS coronavirus outbreaks, no coronavirus research has been done in humans using vitamin C.

Without the guidance of clinical evidence, it is difficult to determine the right timing and dose of IV vitamin C. Case reports and findings from clinical trials will fill these gaps in knowledge.

At the time of this writing, IV vitamin C is being tested in China, Italy, the United States, and other countries across the globe.

We are hopeful that IV vitamin C will be shown to be effective. If so, this information should be quickly shared with front-line doctors.

It is important to note that some medical practices are advertising IV vitamin C as a cure for COVID-19. No scientific evidence supports this claim.

How safe is IV vitamin C?

IV infusions always require proper administration by a medical professional. Patients need to be screened to make sure it is safe for them. Some conditions, like a history of developing kidney stones, might prevent a person from getting IV vitamin C.

From research on vitamin C and cancer, we know that IV vitamin C is safe when medical guidelines are followed.

Stay tuned

We are watching the clinical reports on IV vitamin C and are in touch with the experts on the topic. The Linus Pauling Institute will share results of studies with IV vitamin C as soon as they become available. 📺

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Paul Marik, MD is a physician who developed an IV vitamin C protocol for critical sepsis patients. In personal communications with the LPI, Dr. Marik reports that blood vitamin C levels in some COVID-19 patients are nearly undetectable, making the case for IV vitamin C.

While Marik treats severe COVID-19 patients with IV vitamin C, he always uses it in combination with drugs. This does not support the sole use of IV vitamin C in these situations.

NUTRITIONAL STRATEGIES TO SUPPORT YOUR IMMUNE SYSTEM

Over the age of 50?

Look for the following in your multivitamin supplement:

- 2 mg vitamin B₆
- At least 100 µg of vitamin B₁₂
- 10-15 mg of zinc
- Post-menopausal women and all men should look for a multivitamin without iron.

There is always a good rationale to stay at peak immune function. Beyond the current COVID-19 pandemic, our immune system deals with perennial problems like the seasonal cycles of the common cold and influenza.


The immune system is extremely complex, and its elaborate network of defense mechanisms needs to work properly to be effective.

An abundance of scientific evidence supports the vital role that vitamins, minerals, and other nutrients play in maintaining immune function.

Below is the LPI's **Immune System Foundation**: a list of nutrients that form the base for a healthy immune system. Often, these recommendations can be reached through a **healthy diet** and taking a **daily multivitamin**.

On the next page are the **Immune Essentials**: nutrients of vital importance to the immune system when it is challenged. Consider taking separate dietary supplements for these specific nutrients.

As research about treating COVID-19 with dietary supplements evolves, we may update this list with additional nutrients. At the time of this writing, several phytochemicals are being evaluated for antiviral activity.

We will provide you with an update if and when that information becomes available. 

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<https://lpi.oregonstate.edu/mic/health-disease/immunity>

The Immune System Foundation

The LPI recommendations are for adult men and adult women who are not pregnant or breast-feeding. These recommendations are from food and dietary supplements combined.

Vitamin A (including beta carotene)

Men: 900 µg/day
Women: 700 µg/day

Vitamin B₆

Men and Women:
1.3 mg/day

Vitamin E

Men and Women:
15 mg/day

DHA

Eat oily fish
2 times per week

Vitamin B₁₂

Men and Women:
2.4 µg/day

Folate

Men and Women:
400 µg/day

Copper

Men and Women:
900 µg/day

Selenium

Men and Women:
55 µg/day

Vitamin C

Men and Women:
400 mg/day

Vitamin D

Men and Women:
2,000 IU/day

Iron

Men: 8 mg/day
Women: 18 mg/day
(See note below)

Zinc

Men: 11 mg/day
Women: 8 mg/day

Special note:

Before menopause, women need 18 mg of iron per day. Following menopause, this recommendation decreases to 8 mg per day.

IMMUNE ESSENTIALS

Vitamin C, vitamin D, zinc, and DHA play a special role in immunity. While the usual LPI recommendations for these nutrients can be attained by diet and a daily multivitamin, we recognize that your immune system might face additional challenges at certain times. Dietary supplements are an important strategy to help you stay healthy.

Review the supplement information below and determine whether you should consider extra supplementation. Be sure to note our cautions to avoid taking too much or harmful drug interactions.

Vitamin C

C

up to **2,000 mg**
per day

Immune functions:

Vitamin C is an antioxidant that protects cells against damaging free radicals produced by the immune system. Vitamin C also may increase the production and function of certain immune cells.

Why take a supplement?

Vitamin C can be depleted during a serious illness or infection. Extra vitamin C might be helpful for older adults.

Caution:

More than 2,000 mg of vitamin C a day might cause intestinal gas, bloating, and diarrhea. If you are prone to kidney stones, talk to your doctor before starting any vitamin C supplements.

Zinc

Zn

up to **40 mg**
per day

Immune functions:

Zinc is required for the growth and development of immune cells. Zinc is a structural component of proteins critical for normal immune function. It is also important for the synthesis of antibodies.

Why take a supplement?

Extra zinc might help if you feel a cold coming on. Older adults are more susceptible to zinc deficiency.

Caution:

Try not to exceed 40 mg of zinc a day from a combination of diet and supplements.

Vitamin D

D

up to **4,000 IU**
per day

Immune functions:

Vitamin D increases the production of small peptides and proteins that can damage bacteria or viruses. It also limits the amount of inflammation generated by immune cells in an infection.

Why take a supplement?

Evidence suggests that a daily vitamin D supplement protects against respiratory infection. People who rarely go outside, are severely overweight, wear sunblock, or have dark skin are more likely to have low blood vitamin D levels without supplementation.

Caution:

Vitamin D supplements should be taken daily if possible. Do not take large amounts (greater than 10,000 IU) of vitamin D in a single day unless advised by your doctor.

DHA

DHA

250 mg
per day

Immune functions:

Docosahexaenoic acid is an omega-3 fatty acid also known as DHA. It can be converted into compounds that reduce inflammatory damage caused by bacterial and viral infections.

Why take a supplement?

If you are not eating oily fish 1-2 times per week or taking a supplement, you are likely not getting enough DHA.

Caution:

If you are prone to bleeding or are on blood thinners, consult your doctor before taking DHA supplements. The only vegan source of DHA supplements is from algae oil.



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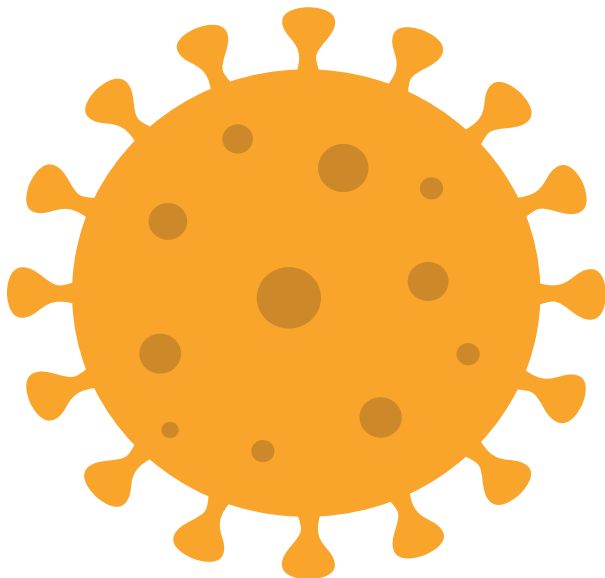
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LINUS PAULING INSTITUTE RESEARCH NEWSLETTER

SPECIAL COVID-19 EDITION



FEATURING

- A New Online Database of COVID-19 Patient Data
- The Facts Surrounding IV Vitamin C in Treating COVID-19
- Nutrients to Help Support Your Immune System