

Is Niacin a Missing Piece of the COVID Puzzle?

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STORY AT-A-GLANCE

- › B vitamins may play an important role in COVID-19 prevention and treatment, according to two recent papers
- › Based on B vitamins' effects on your immune system, immune-competence and red blood cells (which help fight infection), supplementation may be a useful adjunct to other prevention and treatment strategies
- › B vitamins can influence several COVID-19-specific disease processes, including viral replication and invasion, cytokine storm induction, adaptive immunity and hypercoagulability
- › Niacin appears particularly important. According to one published paper, there appears to be a causative link between low niacin status and SARS-CoV-2 infection
- › SARS-CoV-2's ability to invade your body is dependent on calcium signaling, which in turn is dependent on the presence of NAADP, which is formed from niacin. NAADP-dependent calcium signaling is responsible both for the inhibition of viral entry into cells and driving the virus out of already infected cells

This article was previously published January 20, 2021, and has been updated with new information.

While vitamins C and D have garnered much attention in the fight against COVID-19, B vitamins can also play an important role, according to two recent papers – niacin (B3) in particular.

The first, "Be Well: A Potential Role for Vitamin B in COVID-19,"^{1,2} was published in the February 2021 issue of the journal *Maturitas*. The paper is the result of a joint collaboration between researchers at the University of Oxford, United Arab Emirates University and the University of Melbourne, Australia.

While no studies using B vitamins have been performed on COVID-19 patients, the researchers stress that, based on B vitamins' effects on your immune system, immune-competence and red blood cells (which help fight infection), supplementation may be a useful adjunct to other prevention and treatment strategies. As noted by the authors:³

"There is a need to highlight the importance of vitamin B because it plays a pivotal role in cell functioning, energy metabolism, and proper immune function.

Vitamin B assists in proper activation of both the innate and adaptive immune responses, reduces pro-inflammatory cytokine levels, improves respiratory function, maintains endothelial integrity, prevents hypercoagulability and can reduce the length of stay in hospital.

Therefore, vitamin B status should be assessed in COVID-19 patients and vitamin B could be used as a non-pharmaceutical adjunct to current treatments

...

Vitamin B not only helps to build and maintain a healthy immune system, but it could potentially prevent or reduce COVID-19 symptoms or treat SARS-CoV-2 infection. Poor nutritional status predisposes people to infections more easily; therefore, a balanced diet is necessary for immuno-competence."

B Vitamins Play Many Roles in COVID-19 Disease Process

Importantly, B vitamins can influence several COVID-19-specific disease processes, including:⁴

- Viral replication and invasion
- Cytokine storm induction

- Adaptive immunity
- Hypercoagulability

The paper goes on to detail how each of the B vitamins can help manage various COVID-19 symptoms:⁵

Vitamin B1 (thiamine) – Thiamine improves immune system function, protects cardiovascular health, inhibits inflammation and aids in healthy antibody responses. Vitamin B1 deficiency can result in an inadequate antibody response, thereby leading to more severe symptoms. There's also evidence suggesting B1 may limit hypoxia.

Vitamin B2 (riboflavin) – Riboflavin in combination with ultraviolet light has been shown to decrease the infectious titer of SARS-CoV-2 below the detectable limit in human blood, plasma and platelet products.

Vitamin B3 (niacin/nicotinamide) – Niacin is a building block of NAD and NADP, which are vital when combating inflammation.

Vitamin B5 (pantothenic acid) – Vitamin B5 aids in wound healing and reduces inflammation.

Vitamin B6 (pyridoxal 5'-phosphate/pyridoxine) – Pyridoxal 5'-phosphate (PLP), the active form of vitamin B6, is a cofactor in several inflammatory pathways. Vitamin B6 deficiency is associated with dysregulated immune function. Inflammation increases the need for PLP, which can result in depletion.

According to the authors, in COVID-19 patients with high levels of inflammation, B6 deficiency may be a contributing factor. What's more, B6 may also play an important role in preventing the hypercoagulation seen in some COVID-19 patients.

Vitamin B9 (folate/folic acid) – Folate, the natural form of B9 found in food, is required for the synthesis of DNA and protein in your adaptive immune response.

Folic acid, the synthetic form typically found in supplements, was recently found⁶ to inhibit furin, an enzyme associated with viral infections, thereby preventing the SARS-CoV-2 spike protein from binding to and gaining entry into your cells. The research⁷ suggests folic acid may therefore be helpful during the early stages of COVID-19.

Another recent paper⁸ found folic acid has a strong and stable binding affinity against SARS-CoV-2. This too suggests it may be a suitable therapeutic against COVID-19.

Vitamin B12 (cobalamin) – B12 is required for healthy synthesis of red blood cells and DNA. A deficiency in B12 increases inflammation and oxidative stress by raising homocysteine levels. Your body can eliminate homocysteine naturally, provided you're getting enough B9 (folate), B6 and B12.⁹

Hyperhomocysteinemia – a condition characterized by abnormally high levels of homocysteine – causes endothelial dysfunction, activates platelet and coagulation cascades and decreases immune responses.

B12 deficiency is also associated with certain respiratory disorders. Advancing age can diminish your body's ability to absorb B12 from food,¹⁰ so the need for supplementation may increase as you get older. According to "Be Well: A Potential Role for Vitamin D in COVID-19":¹¹

"A recent study showed that methylcobalamin supplements have the potential to reduce COVID-19-related organ damage and symptoms. A clinical study conducted in Singapore showed that COVID-19 patients who were given vitamin B12 supplements (500 µg), vitamin D (1000 IU) and magnesium had reduced COVID-19 symptom severity and supplements significantly reduced the need for oxygen and intensive care support."

Niacin – A Missing Piece of the COVID-19 Puzzle?

The second paper,¹² "Sufficient Niacin Supply: The Missing Puzzle Piece to COVID-19 and Beyond?" (which is a preprint and has yet to undergo peer review), focuses specifically on niacin (B3), raising the question of whether this vitamin might actually be a crucial player in the COVID-19 disease process. As noted in the abstract:

"Definitive antiviral properties are evidenced for niacin, i.e., nicotinic acid (NA), as coronavirus disease 2019 (COVID-19) therapy for both disease recovery and prevention, to the level that reversal or progression of its pathology follows as an intrinsic function of NA supply.

This detailed investigation provides a thorough disentanglement of how the downstream inflammatory propagation of ensuing severe acute respiratory virus 2 (SARS-CoV-2) infection is entirely prohibited or reversed upstream out the body to expeditiously restore health with well-tolerated dynamic supplementation of sufficient NA (i.e., ~1-3 grams per day)."

As noted in this paper, a primary hallmark of COVID-19 pathology is the cytokine storm, which can lead to multiple organ failure and death. Marked elevations in proinflammatory cytokines are to blame for this chain of events, most notable of which are interleukin-6 (IL-6), interleukin-1 β (IL-1 β), tumor necrosis factor- α (TNF- α) and monocyte chemoattractant protein-1 (MCP-1).

If you can decrease and control these damaging cytokines, you stand a good chance of thwarting the cytokine storm and the downstream damage it causes. Nicotinamide adenine dinucleotide (NAD⁺) plays an important role in this, and niacin is a building block of NAD. As explained in "Be Well: A Potential Role for Vitamin D in COVID-19":¹³

"NAD⁺ is released during the early stages of inflammation and has immunomodulatory properties, known to decrease the pro-inflammatory cytokines, IL-1 β , IL-6 and TNF- α . Recent evidence indicates that targeting IL-6 could help control the inflammatory storm in patients with COVID-19."

Aside from markedly decreasing proinflammatory cytokines, niacin has also been shown to:¹⁴

- Reduce the replication of a number of viruses, including vaccinia virus, human immunodeficiency virus, enteroviruses and hepatitis B virus
- Reduce neutrophil infiltration
- Have anti-inflammatory effect in patients with ventilator-induced lung injury

Niacin Modulates the Bradykinin Storm

COVID-19 also triggers bradykinin storms. Bradykinin is a chemical that helps regulate your blood pressure and is controlled by your renin-angiotensin system (RAS). The bradykinin hypothesis provides a model that helps explain some of the more unusual symptoms of COVID-19, including its bizarre effects on your cardiovascular system.

Researchers have discovered SARS-CoV-2 downregulates your body's ability to degrade or break down bradykinin. The end result is a bradykinin storm, and this appears to be an important factor in many of COVID-19's lethal effects, perhaps even more so than the cytokine storms associated with the disease. As bradykinin accumulates, the more serious COVID-19 symptoms appear.

Vitamin D has a significant impact on the RAS,¹⁵ and can therefore help prevent a bradykinin storm, but niacin also plays an important role. As noted in "Sufficient Niacin Supply: The Missing Puzzle Piece to COVID-19 and Beyond?":¹⁶

"Immediate-release NA [niacin] administration has been reported as highly effective in preventing the lung tissue damage involved in this ... pathology. As a matter of fact, authors of a March, 2020, paper¹⁷ in Nature for this very reason conclude with suggestion of niacin supplementation to COVID-19 patients as a 'wise approach.'"

The paper also expounds on the role of NAD+, and why niacin is a useful strategy for boosting NAD+:¹⁸

"The major effects of COVID-19 are evidenced to involve tryptophan metabolism and the kynurenine pathway towards depletions of these

precursors of NAD+ ...

Exclusively sufficient dosage of immediate-release NA – through its processing in the mammalian body to form NAADP [nicotinic acid adenine dinucleotide phosphate, a calcium mobilizer] – leads to an inverse potential energy pump back upstream, from the core up and ultimately out the body, of the downstream ensuing propagation of such inflammatory disease that spreads into the cells.

This is made possible by the capability of NAADP to be readily formed by sufficient NA supply to induce Ca²⁺ [calcium] channeling back upstream out the body of built-up or ensuing inflammation, representing kinetic energy ... that by electron gradient, moves downstream into the body.

Attempting to restore NAD+ with other NAD+-precursors aside from NA (e.g., nicotinamide, nicotinamide riboside, nicotinamide mononucleotide) only actually temporarily and in a sense, artificially, raises NAD+ levels, until they imminently deplete back down with further ensuing inflammation.

NA is in fact the only compound to readily produce NAADP if needed in acidic environments (as is characteristic to ensuing inflammatory disease pathology), which in turn provides a potential energy/H⁺ pump-out action of its inverse, downstream kinetic (heat) energy inflammation to ultimately restore NAD+ to normal, pre-inflammatory levels, as well as other inflammatorily-depleted cofactors and biochemical pathways towards a more thermodynamically homeostatic health status ...

The 'niacin red flush' in fact is this thermodynamic exfoliation of ensuing disease, toxins, and (restoration of) free radical-damaged compounds being H⁺ (potential energy) pumped out the body.

It represents the anti-inflammatory or thermodynamic (i.e., energy transfer-like) therapy in action that only and exclusively sufficient oral intake of immediate-release NA is capable of (readily) accomplishing with potency."

Recommended Use

The paper¹⁹ goes deep into the biochemical aspects of how niacin works in your body, so if you're interested in that, you may want to read through it. In summary, as it pertains to COVID-19, the important thing to understand is that there appears to be a causative link between low niacin status and SARS-CoV-2 infection.

“ Nothing outside of sufficiently ... supplied niacin is capable of readily leading to the NAADP supply needed ... for therapeutic action that counteracts inflammatory disease progression.”

According to the authors, SARS-CoV-2's ability to invade your body is dependent on whether calcium signaling can properly proceed, which in turn is dependent on the presence of NAADP. And, as explained in the quoted section above, niacin forms NAADP in your body. NAADP-dependent calcium signaling is responsible both for the inhibition of viral entry into cells and driving the virus out of already infected cells.

And, again, the authors stress that "nothing outside of sufficiently, dynamically supplied niacin is capable of readily leading to the NAADP supply needed in these acidic environments for therapeutic action that counteracts inflammatory disease progression."

They also point out that the flushing you get from niacin is part of how the niacin drives inflammatory free radicals out of the cells. As you continue to take the supplement at a consistent, sufficiently high dose, that flushing will gradually lessen, which is a sign that your body is reaching a healthy homeostasis.

"This represents perhaps the ideal state that should be worked up to and maintained thereafter – in terms of niacin dosing – to respectively reverse out and prevent inflammation," the authors state.²⁰

While the flushing can be uncomfortable, the authors stress that it is "indeed safe," and actually "should be sought when needed for its anti-inflammatory properties."

Suggested Dosing

As a "health restorative therapy" for those diagnosed with SARS-CoV-2, they recommend starting with a dose of 500 milligrams of immediate-release niacin, two to three times a day, ideally within the first 48 hours of symptom onset. As your flush response lessens, increase your dose to 1,000 mg, two to three times a day.²¹

"For the subgroup of patients still suffering with high cytokines profiles from deep, remnant damage of previously experienced SARS-CoV-2 infection – termed the 'long-haulers' – alleviation from ailment(s) towards complete health restoration to pre-infection state from initiating and maintaining the aforementioned dosage regimen has consistently been reported to assume within two days and to incrementally follow further over the course of weeks."²²

Although the authors suggest you can use niacin prophylactically, using that same dose, I disagree. According to the authors:²³

"By readily providing sufficient NAADP, this same NA dosage regimen is capable of serving as prophylaxis, which can be interpreted as the physical/biochemical inability of sufficient progression of SARS-CoV-2 in order to enter into the body and/or thereafter induce replication, infection onset, or disease progression in a previously uninfected host."

There may be some value to the high doses in acute COVID-19 infections but I am skeptical. I am a huge fan of NAD+ augmentation and have been using it for years. My research suggests you really only need about 25 mg per day of niacin, which will not cause flushing in nearly anyone. I believe most would benefit from taking 25 mg of niacin daily, preferably in a well-balanced B complex, which would have thiamine (B1) that has also been shown to be useful in COVID-19.

Other alternatives to high-dose niacin would be nicotinamide riboside (NR) and nicotinamide mononucleotide (NMN), which is my personal favorite. I believe that compounding these into rectal suppositories would avoid most of the methylation of the supplement and supply you with higher NAD+ tissue levels.

Another downside of high-dose niacin is that it breaks down to nicotinamide and in high doses, nicotinamide will inhibit Sirt1, which is an important longevity protein.

Personally, I believe a superior strategy to high-dose niacin in acute COVID-19 would be to use nebulized hydrogen peroxide at 0.1%. I have never seen or heard of this intervention failing in the treatment of COVID-19.

Starting Peroxide Concentration	Hydrogen Peroxide	+	Normal Saline	=	Ending Peroxide Concentration
3%	1/4 tsp	+	7 1/4 tsp	=	.1%
12%	1/4 tsp	+	5 ounces	=	.1%
36%	1/4 tsp	+	15 ounces	=	.1%

How to Improve Your Vitamin B Status

As a general rule, I recommend getting most if not all of your nutrition from real food. This will work well for most B vitamins, but not if you're using niacin therapeutically, as described above. For that, you will need to take a supplement.

That said, the list below will show you which foods contain which B vitamins, as well as provide general guidance on dosage if you're taking a supplement. If you're trying to improve your vitamin B status, also consider limiting sugar and eating more fermented foods.

The reason for this is because the entire B group vitamin series is produced within your gut, assuming you have healthy gut flora. Eating real food, including plenty of leafy greens and fermented foods, will provide your microbiome with important fiber and beneficial bacteria to help optimize your internal vitamin B production.

Nutrient	Dietary Sources	Supplement Recommendations
Vitamin B1	Pork, fish, nuts and seeds, beans, green peas, brown rice, squash, asparagus and seafood. ²⁴	The recommended daily allowance for B1 is 1.2 mg/day for men and 1.1 mg/day for women. ²⁵
Vitamin B2	Eggs, organ meats, lean meats, green vegetables such as asparagus, broccoli and spinach. ²⁶	The RDA is 1.1 mg for adult women and 1.3 mg for men. Your body cannot absorb more than about 27 mg at a time, and some multivitamins or B-complex supplements may contain unnecessarily high amounts. ²⁷

Nutrient

Dietary Sources

Supplement Recommendations

Vitamin B3

Liver, chicken, veal, peanuts, chili powder, bacon and sun-dried tomatoes have some of the highest amounts of niacin per gram.²⁸

Other niacin-rich foods include baker's yeast, paprika, espresso coffee, anchovies, spirulina, duck, shiitake mushrooms and soy sauce.²⁹

The dietary reference intake established by the Food and Nutrition Board ranges from 14 to 18 mg per day for adults.

Higher amounts are recommended depending on your condition. For a list of recommended dosages, see the Mayo Clinic's website.³⁰

The dosage recommended as an anti-inflammatory, health-restorative therapy in "Sufficient Niacin Supply: The Missing Puzzle Piece to COVID-19 and Beyond?"³¹ is 500 mg two to three times a day, working your way up to 1,000 mg, two to three times a day as the flushing lessens.

Nutrient	Dietary Sources	Supplement Recommendations
Vitamin B5	Beef, poultry, seafood, organ meats, eggs, milk, mushrooms, avocados, potatoes, broccoli, peanuts, sunflower seeds, chickpeas and brown rice. ³²	The RDA is 5 mg for adults over the age of 19. Pantothenic acid in dietary supplements is often in the form of calcium pantothenate or pantethine. ³³
Vitamin B6	Turkey, beef, chicken, wild-caught salmon, sweet potatoes, potatoes, sunflower seeds, pistachios, avocado, spinach and banana. ^{34,35}	Nutritional yeast is an excellent source of B vitamins, especially B6. ³⁶ One serving (2 tablespoons) contains nearly 10 mg of vitamin B6. Not to be confused with Brewer's yeast or other active yeasts, nutritional yeast is made from an organism grown on molasses, which is then harvested and dried to deactivate the yeast. It has a pleasant cheesy flavor and can be added to a number of different dishes.

Nutrient

Dietary Sources

Supplement Recommendations

Vitamin B9

Fresh, raw, organic leafy green vegetables, especially broccoli, asparagus, spinach and turnip greens, and a wide variety of beans, especially lentils, but also pinto beans, garbanzo beans, kidney beans, navy and black beans.³⁷

Folic acid is a synthetic type of B vitamin used in supplements; folate is the natural form found in foods.

(Think: Folate comes from foliage, edible leafy plants.)

For folic acid to be of use, it must first be activated into its biologically active form (L-5-MTHF).

Nearly half the population has difficulty converting folic acid into the bioactive form due to a genetic reduction in enzyme activity.

For this reason, if you take a B-vitamin supplement, make sure it contains natural folate rather than synthetic folic acid.

Nutritional yeast is an excellent source.³⁸

Nutrient

Dietary Sources

Supplement Recommendations

Research³⁹ also shows your dietary fiber intake has an impact on your folate status.

For each gram of fiber consumed, folate levels increased by nearly 2%.

The researchers hypothesize that this boost in folate level is due to the fact that fiber nourishes bacteria that synthesize folate in your large intestine.

Nutrient	Dietary Sources	Supplement Recommendations
Vitamin B12	<p>Vitamin B12 is found almost exclusively in animal tissues, including foods like beef and beef liver, lamb, snapper, venison, salmon, shrimp, scallops, poultry, eggs and dairy products.</p> <p>The few plant foods that are sources of B12 are actually B12 analogs that block the uptake of true B12.</p>	<p>Nutritional yeast is high in B12, and is highly recommended for vegetarians and vegans.</p> <p>One serving (2 tablespoons) provides nearly 8 mcg of natural vitamin B12.⁴⁰</p> <p>Sublingual (under-the-tongue) fine mist spray or vitamin B12 injections are also effective, as they allow the large B12 molecule to be absorbed directly into your bloodstream.</p>

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