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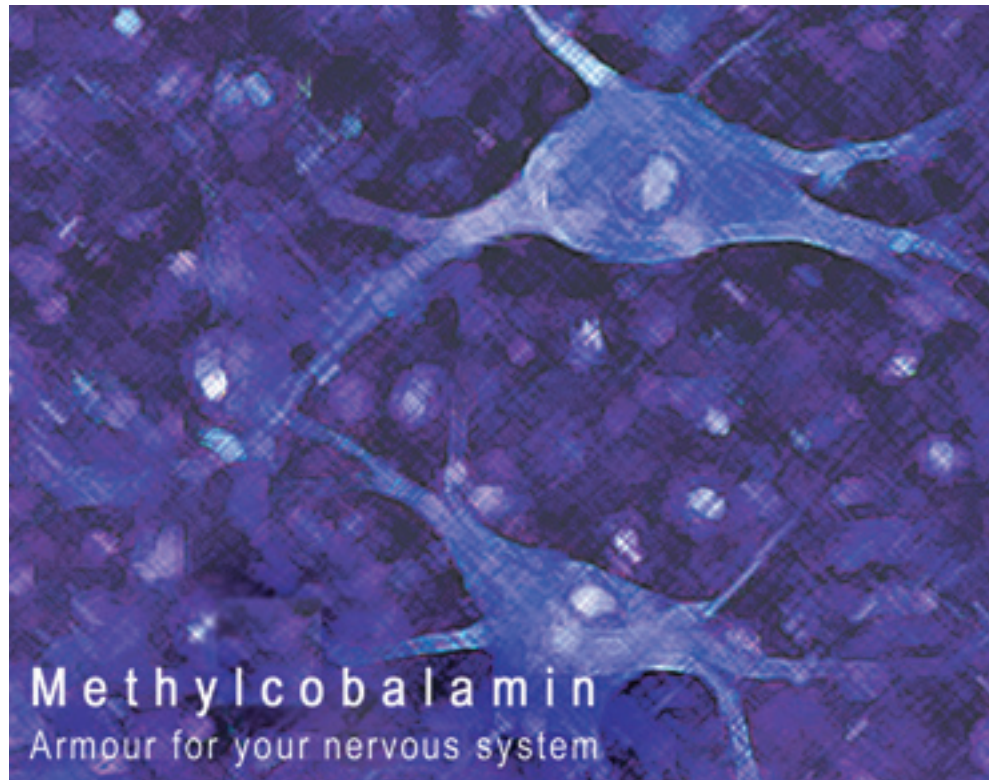
Orthomolecular

The Holistic Lifestyle

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Methylcobalamin is the coenzyme form of vitamin B12 which supports the healthy structure and function of the nerves and brain.

Say that to nearly any health-conscious person you know, and you'll be met with confusion. In most cases, they will simply have no idea what you're babbling about. "Coenzyme vitamin B12?" they'll ask. "Is that sort of like Coenzyme Q10?" And in most other cases, the person will almost know what you're talking about – but not quite. "Coenzyme vitamin B12?" they'll say. "You mean adenosylcobalamin [also known as cobamamide or dibenzocoid], don't you? What's this Methylcobalamin stuff?"

Let's Start at the Very Beginning...

A **coenzyme** is a factor needed for the effective functioning of one of the body's vital enzymes. Many vitamins are not biologically active in the form in which they are normally found in food, but are instead used by the body as part of a coenzyme. In other words, in many cases, **the body has to convert a vitamin into its coenzyme form in order for the vitamin to exert its biological function** (see sidebar, **Enzymes and Coenzymes**).

Or, in the case of vitamin B12: not *function*, but *functions*.

The body uses vitamin B12 in the form of

Welcome Readers

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Holistic International, manufacturers and distributors of the most exciting lines of envelope-pushing nutritional supplements in Canada, welcomes you to this issue of *The Holistic Lifestyle*, published bimonthly. *The Holistic Lifestyle* is designed to provide important information and news of breakthrough research. By providing clearly-written articles, and the primary sources on which they are based, we hope to help you further your own research, assisting you to make the best supplement and lifestyle choices to meet your unique health goals.

The Holistic Lifestyle also provides news about Holistic International and its products, along with trade shows, retailer information, and government regulations and their impact on your health freedom.

Comments? Questions?
We want to hear from you!

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two *different* coenzymes, each of which plays a *different* role in the body. Adenosylcobalamin was discovered earlier, and is the better-known of these coenzymes.

Methylcobalamin is the *other* coenzyme form of B₁₂. It's **Methylcobalamin**, and not adenosylcobalamin, which prevents the creeping numbness, dementia, and spongy degeneration of the nerve cells (**neurons**) seen in B₁₂ deficiency. Adenosylcobalamin does a totally separate set of jobs, helping the body to process some amino acids and to form substances used in the body's energy cycle. One coenzyme can't substitute for the other, any more than you can use your house keys to start your car (see sidebar, **Enzymes and Coenzymes**).

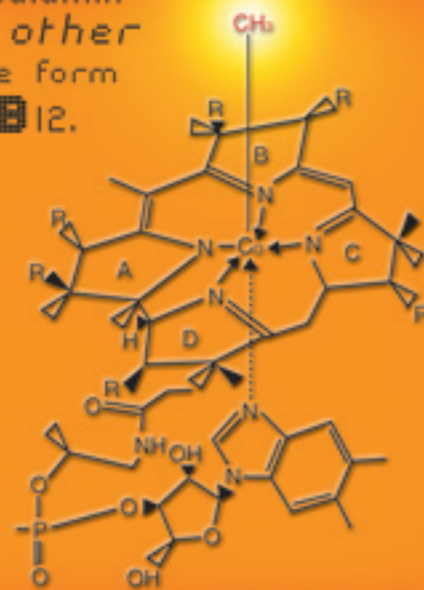
You might think that this is the kind of obscure little factoid that gets put into biology textbooks or turns up on *Who Wants to be a Millionaire?*, but which has no real-world importance. "My diet and supplement program includes plenty of B₁₂," you might think, "so my body will make all the **Methylcobalamin** I could ever want or need."

Like the old song says, *It ain't necessarily so*. While a good diet and supplement program guarantees the body a generous supply of adenosylcobalamin (unless you have a deadly genetic defect), the same cannot be said of **Methylcobalamin**.

The Miserly Liver

Here's the problem. While adenosylcobalamin is readily stored up in the liver (and, to a lesser extent, the kidneys and other tissues), **Methylcobalamin's** job requires that it be free to circulate in body fluids like **cytosol** (the liquid medium of the cell), plasma, and the fluid that bathes the brain and spinal cord (**cerebrospinal fluid**).

Methylcobalamin is the other coenzyme form of B₁₂.



Because of this, **Methylcobalamin** doesn't hang around in the body for very long.

Thus, while a person getting enough of the basic vitamin (cobalamin) will always have plenty of *adenosylcobalamin*, the nervous system has no special store of protective **Methylcobalamin** on which to rely. In fact, the body's **Methylcobalamin** "fuel tanks" can easily be brought below optimal levels, and the supply is quickly depleted if it is not constantly replenished.

And while the body does have some ability to interconvert the different coenzyme forms B₁₂, plenty of evidence shows that, even in "normal" folks, the *balance* of **Methylcobalamin** and adenosylcobalamin can be lost, leading to a **Methylcobalamin** "famine" even the midst of a "feast" of adenosylcobalamin. For instance, several studies¹⁻³ have found that **people can have neurological signs and symptoms of a specific Methylcobalamin deficiency, even when serum B₁₂, and blood tests which measure adenosylcobalamin activity, are perfectly normal.**

Fortunately, evidence has been piling up for nearly three decades that the converse is

Methylcobalamin

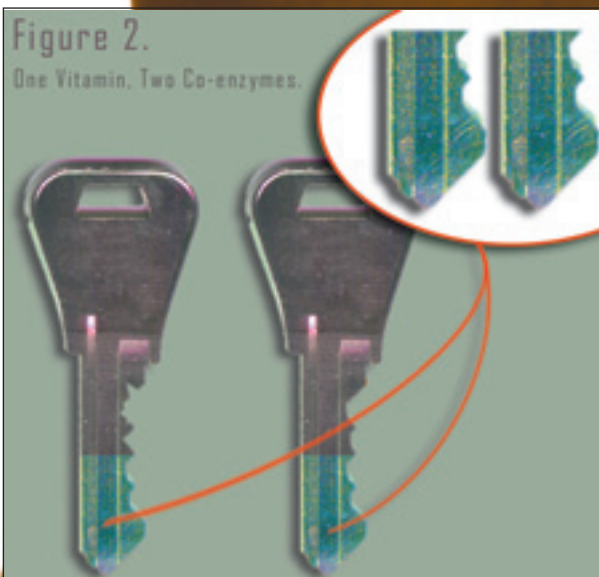
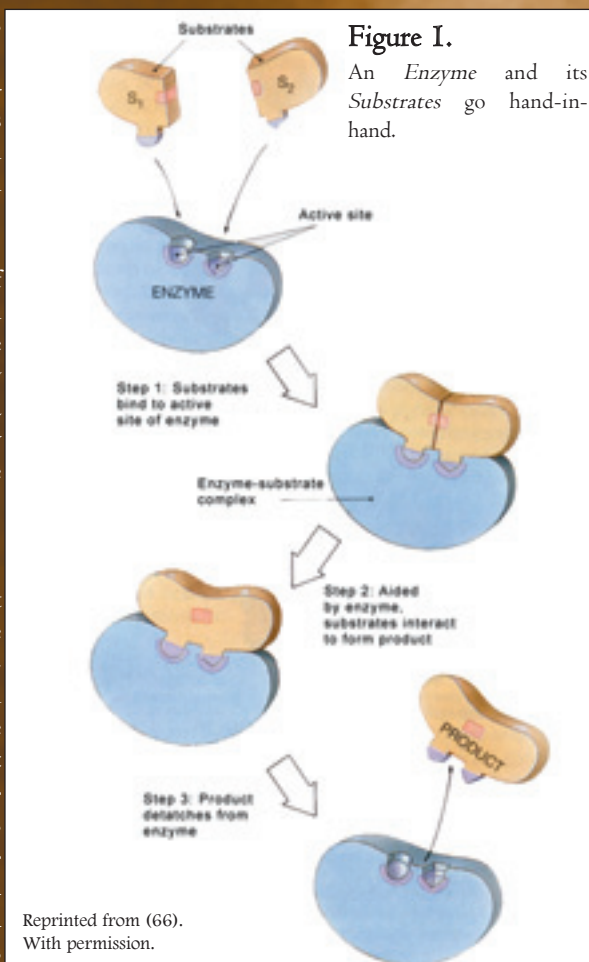
Armour For Your Nervous System

Enzymes and Coenzymes

When someone says “enzymes,” many of us think first of *digestive* enzymes: the specialized molecules which help us break down our food into manageable, absorbable units. But the fact is, nearly every metabolic process in your body is driven by enzymes. Enzymes help make sure that chemical reactions which are necessary to bodily function happen. And while some enzymes in the body tear things down, others build new things up. Everything made by your body — from the **collagen** in your skin and bones to the complex crystals that make up the lens of the eye — is crafted using enzymes.

Each enzyme has an **active site**: a specialized place into which it fits the raw materials (**substrates**) with which it was designed to work. The specialized structure of an enzyme ensures that only the *specific* substrates with which it is designed to work can fit into its active site (see **Figure 1**). This is sometimes referred to as an enzyme’s “**lock-and-key**” specificity. Like any good key, an enzyme opens up one specific lock, and no other.

A **coenzyme** is a factor needed for the effective functioning of one of the body’s enzymes. Without its coenzyme, a given enzyme isn’t complete, and can’t do its job. Many vitamins are not biologically active in the form in which they are normally found in food, but are instead used by the body to make a coenzyme. In other words, **the body has to convert many vitamins into their coenzyme forms in order for those vitamins to exert their biological functions.**



Thus, the body doesn’t *actually use* **niacinamide** (vitamin B₃) to accomplish any biological function: instead, to use B₃, the body must first convert it into its coenzyme form, which is NADH. Likewise, **pantothenic acid** (vitamin B₅) has no biological activity until it is transformed into **Pantethine**, which is quickly used by the body’s cells to make **coenzyme A (CoA)** biologically active.

In the case of vitamin B₁₂, one vitamin is used to make *two different* coenzymes: **adenosylcobalamin** and **Methylcobalamin**. Think of it as two different keys which share a few common teeth. On the one hand, neither key can open the door for

which it was designed if it’s lacking those teeth; but at the same time, neither key can open the *other* key’s matching lock, because each key also has teeth which are *not* held in common with the other (see **Figure 2**).



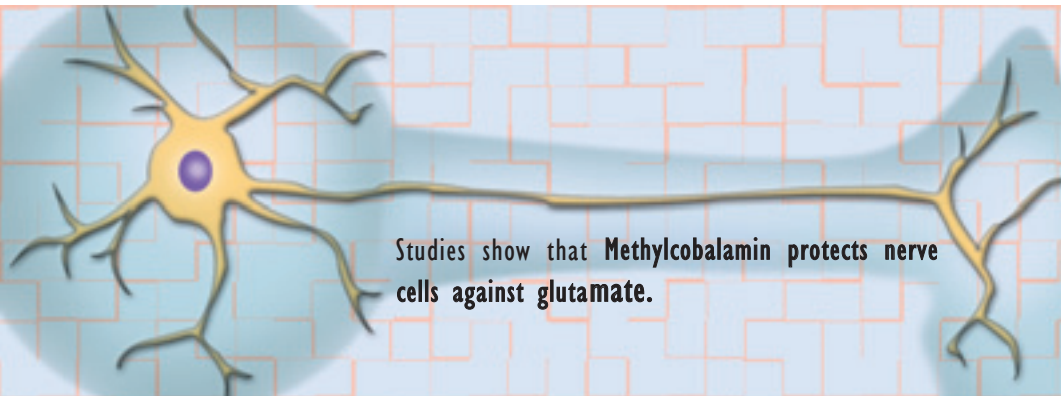
also true. For while healthy people need just a tiny trace of **Methylcobalamin** to avoid a frank deficiency, a massive body of evidence powerfully supports the conclusion that **supplementing with megadose levels of Methylcobalamin** –

nitroprusside (which releases **cyanide** into the cell and simultaneously causes the formation of the virulent **peroxynitrite** free radical).⁸

In addition to *protecting* neurons against

excitement in your life is a great thing, *too much* excitement can get out of control, leading to accidents which can range from the comical – to the deadly.

So it is with glutamate. *Overstimulation* of neurons by this essential neurotransmitter is called **excitotoxicity**, and these power surges can fry your neurons like so many old toasters. So it's hardly surprising to find extensive evidence suggesting that **glutamate excitotoxicity is at the root of a great deal of the degeneration of the brain and nervous system in major neurodegenerative diseases like Multiple Sclerosis (MS),¹⁴⁻¹⁶ Alzheimer's disease,¹⁷⁻²⁰ Parkinson's disease,²⁰⁻²⁴ and Lou Gehrig's disease (ALS).^{25,26}** Glutamate excitotoxicity may also play a role in **damage to the neuroretinal system** in diabetics.²⁷⁻²⁹



and not regular B₁₂ – can protect brain and nerve cells against toxins, help the healing of damaged neurons, and even provide powerful nutritional support in serious neurodegenerative diseases like diabetic neuropathy, Bell's Palsy, multiple sclerosis (MS), Lou Gehrig's Disease (ALS), Alzheimer's disease, normal-tension glaucoma, and perhaps tinnitus, lumbar spinal stenosis, and Parkinson's disease. Again, these benefits are achieved even in cases where there is no simple "deficiency" of dietary B₁₂, and in situations where regular B₁₂ supplements are without effect.

damage from toxic environments, animal studies show that **Methylcobalamin helps regenerate** nerve cells after they've been **crushed,^{7,9-11} compacted,¹² or damaged by toxins like acrylamide** (a substance used to make synthetic fabrics which happens to be a deadly toxin to your nervous system).¹³

So what does the body use to defend its nerve cells against the ravages of unfettered glutamate?

Right the first time.

Shielding the Brain and Nerves

In animal and test-tube studies, **Methylcobalamin has been shown to protect nerve cells against a wide variety of hostile environmental situations, including lack of vital cellular fuel,⁴ thiamine deficiency** (which normally causes degeneration of the nervous system, leading to loss of reflexes in the extremities, racing heartbeat, loss of coordination, confusion, apathy, and memory loss),⁵ **oxygen starvation,⁴ and exposure to toxins like methylmercury** (the especially toxic, bioaccumulative form of mercury which contaminates fish),⁶ **botulin** (the bacterial toxin that causes the paralyzing nerve damage in **botulism**),⁷ or

Several of these effects were specifically shown to be dose-dependent² – that is, **the more Methylcobalamin the nerves cells got, the higher their level of protection.⁴** And the B₁₂ in your multivitamin? When added directly to the nerve cell culture, studies show that **regular B₁₂ supplements can't provide the neuroprotective and neuroregenerative benefits of Methylcobalamin.**^{4,8,9}

Studies show that **Methylcobalamin protects nerve cells against glutamate's excitotoxic hazards,** whether **Methylcobalamin** is added directly to isolated neurons^{30,31} or is given to live animals before removing the nerve cells and exposing them to the hazard.⁴ Direct administration of cyanocobalamin (the B₁₂ in your multivitamin) has no protective effect.⁴ But, of course, it's a big jump from the protection of nerve cells against a particular toxic environment, and demonstrating actual benefits in people suffering with neurological diseases. The nutraceutical world is littered with supplements which "ought" to work, but which have no proof to back them, or which have been tried and ultimately found wanting.

Thrilled to Death

When it comes to the protection of neurons, however, one particular kind of hazard stands out. **Glutamate** is the most important "excitatory" messenger molecule (**neurotransmitter**) in the brain – that is, it's the main brain chemical involved in "exciting" neurons into action. The "turning on" of special "switches" in the brain (**NMDA glutamate receptors**) by glutamate is crucial to the formation of long-term memories, among other things. But as everyone knows, while having a little

Fortunately, you don't have to guess about the efficacy of **Methylcobalamin** in these disorders. Wherever it's been tested,

Methylcobalamin

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clinical trials have found that **Methylcobalamin** provides powerful support in terrifying disorders of the brain and nervous system.

Paralyzing Viruses

Peripheral facial paralyses (including **Bell's palsy** and **Ramsay Hunt's syndrome** [or "herpes zoster oticus"]) are now believed to be caused by the sudden reactivation of viruses (or certain other pathogens) which had previously been kept at bay by the body's immune system. The viruses infect and inflame the nerves which control the muscles of the face, and the face becomes paralyzed on one side. It's a terrifying, frustrating ordeal.

Several groups of scientists have investigated the use of **Methylcobalamin** in Bell's palsy, and they have uniformly found that **Methylcobalamin** speeds the **recovery of normal nerve functioning**. Dr. Hideto Kobayashi and his colleagues gave **Methylcobalamin** to a group of 39 patients with Bell's palsy or Ramsay Hunt's syndrome, and compared their progress to that seen in a group of 21 patients who received the regular therapies for these diseases (including the steroid drug **prednisone**, which remains the most common treatment for Bell's palsy). **The people who took Methylcobalamin recovered more quickly**, their facial paralysis scores normalizing in less time, and their **stapedial reflex** (an involuntary contraction of the muscles around the

stirrup of the ear, which protects the inner ear from loud sounds by tightening the eardrum) returning more quickly to those who had lost it. The team reported that **Methylcobalamin "was considered to be effective in the treatment of peripheral facial palsy."**³²

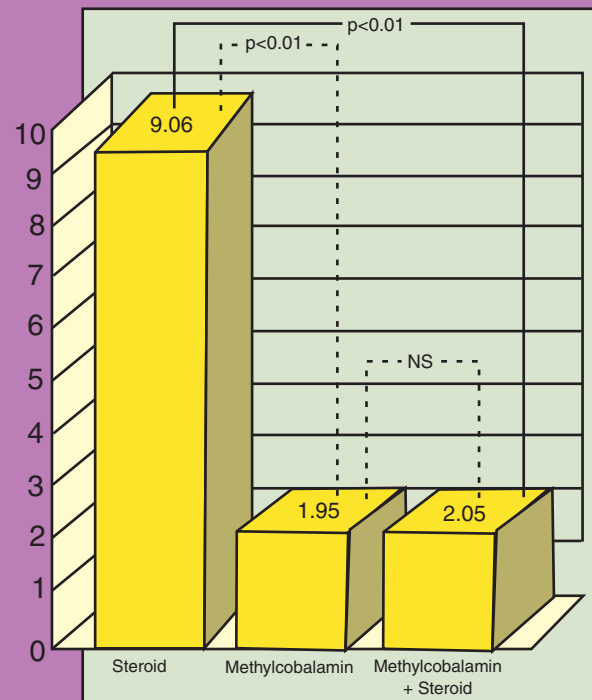
Two groups of scientists ran trials^{33,34} in which patients with Bell's palsy were given either prednisone alone, **Methylcobalamin** alone, or the drug and the coenzyme together. Both trials found that **the time required for complete recovery was significantly shorter for people who took Methylcobalamin (whether by itself or in combination with prednisone) than for those who took the steroid drug alone**. In fact, while in both trials the patients receiving the steroid drug alone took an average of about 67 days to completely recover the function of their facial muscles, **patients in the later trial who took Methylcobalamin averaged just two weeks to complete recovery**.³⁴ Adding the steroid to **Methylcobalamin** supplements did not lead to faster recovery than taking **Methylcobalamin** alone.

Interestingly, the groups receiving **Methylcobalamin** in the later of

the two trials³⁴ recovered much more quickly than the equivalent groups in the earlier trial.³³ The reason might be that the latter trial³⁴ took special care to **make sure that the Bell's palsy patients got their Methylcobalamin within two weeks of**

Figure 3
Redrawn from (34).

Average time (weeks) required for complete recovery of facial nerve functions.



their first attack. Similarly, the effectiveness of some *drug* therapies for peripheral facial paralysis have been found to be heavily dependent on catching the damage early.³⁵

Multiple Sclerosis (MS)

In a pilot trial,³⁶ six people with degenerating MS received 60 milligrams of **Methylcobalamin** a day. The scientists compared the changes which took place in the patients' nerve function (measured by nerve responses to mild electrical stimulation) over the course of up to two years before the trial began, to the changes which happened during the six months in which the patients took **Methylcobalamin**. They

Those who
took **Methylcobalamin**
averaged just
two weeks to
complete recovery.



found that there was a significant *reversal* of the direction of changes in nerve function while patients took Methylcobalamin. Before Methylcobalamin, about one fifth of all measurements of nerve function suggested

While 59% of glaucoma patients not taking Methylcobalamin experienced worsening sight, 86% of patients taking Methylcobalamin experienced no loss of function.

that the nerves were degenerating. While the patients were supplementing with Methylcobalamin, however, only half as many nerve measurements showed signs of degeneration. And while, in the time before the trial began, just 4% of the nerve measurements suggested that the nerve in question had improved, 18%, or four-and-a-half times as many nerve readings showed signs of improvement while patients were taking Methylcobalamin.

Lou Gehrig's Disease

In a randomized, double-blind, controlled trial,³⁷ 24 patients with Amyotrophic Lateral Sclerosis (ALS), better known as Lou Gehrig's disease, took megadoses of Methylcobalamin through intramuscular injection for just under a month at one of two doses (25 milligrams or 500 micrograms a day). Patients who took the higher dose of Methylcobalamin experienced increases in measurements of their nerves' ability to trigger responses in the muscles. Two patients' gaits were also noted to improve in the higher-dose group. The scientists running the trial concluded that Methylcobalamin "may provide a clinically useful measure to improve or retard muscle wasting, if a larger extended trial fulfills its promise."

Alzheimer's Disease

When patients with Alzheimer's disease and related dementias are given regular (cyanocobalamin) B₁₂ supplements, no improvement in mental function is seen, even in cases who *do* have low

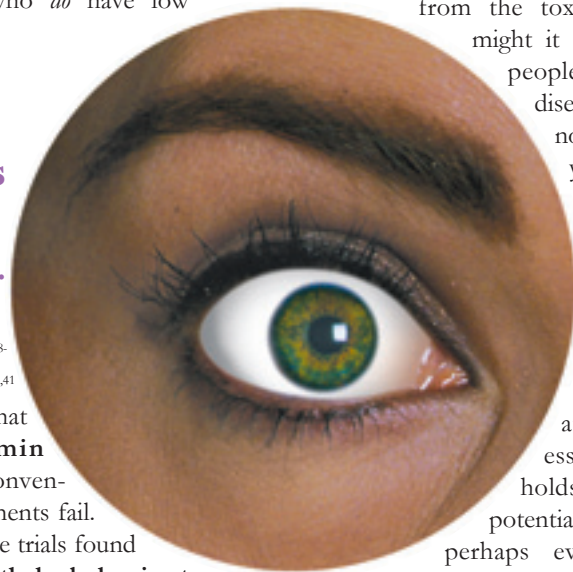
serum B₁₂ levels.³⁸⁻³⁹ Yet two trials^{40,41} have reported that Methylcobalamin works where conventional B₁₂ supplements fail. Between them, the trials found that giving Methylcobalamin to people with Alzheimer's disease or related dementias (like Pick's disease) leads patients to have better interaction with other people and with the world around them, while improving mood and relieving neurological symptoms. The patients' families and physicians also found them to be improved. The findings in these trials on intellectual functioning were inconsistent: some scales showed improvements, but others did not. Both of these trials, however, used relatively low doses of Methylcobalamin compared to what's been found successful in other disorders. A higher dose, more typical of that used in other advanced neurological diseases like ALS, might be expected to give more consistently positive results.

A Good Guess: Parkinson's Disease

As noted above, there's good reason to believe that Parkinson's disease is caused and/or accelerated by glutamate excitotoxicity. Drugs which lower glutamate levels, or which "tune down" its receptor, improve many of the

symptoms of the disease,^{21,22,23} while drugs which stimulate the receptor make them worse.²⁴

So if Methylcobalamin protects neurons from the toxicity of glutamate, might it provide support for people with Parkinson's disease? Unfortunately, no clinical trials have yet been run to test this idea. But granted how safe Methylcobalamin supplements have proven to be, and its clear benefits in other neurodegenerative diseases, this essential coenzyme holds out hope as a potential way to prevent, and perhaps even to treat, this debilitating disease.



Caramelized Nerves

About 60% of people with diabetes will develop diabetic neuropathy, a kind of nerve damage in which the constant exposure of the nerves to high levels of glucose literally caramelizes (glycates) their proteins, a process which warps their structure and impedes their function.

A string of clinical trials have reported that Methylcobalamin improves nerve function in people with diabetic neuropathy, as demonstrated by things like improvements in the ability to detect gentle vibration,^{42,43} reduced tingling, numbness, and pain in the extremities,^{44,45} less strong sensations of "heaviness" in the legs,⁴⁵ and the restoration of neurons' ability to efficiently transmit a signal^{42,44} and to properly regulate the heartbeat.^{43,46,47} Trials which have looked at overall improvement in patients' neuropathic symptoms and signs have also reported remarkably positive results.^{42,45,48,49}

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Eyes Under Pressure

Glaucoma is a major cause of loss of vision, caused by damage to the nerves leading out from the eyes to the brain. The nerve damage results from excessive stress placed on the neurons by the fluid pressure inside the eyeball, despite the fact that, in about a third of people with glaucoma, the pressure in the eye is within the “normal” range. Such people are said to have “normal-tension glaucoma.”

In a controlled study, 14 patients with normal-tension glaucoma were treated with **Methylcobalamin**, and their progress was compared with that of 22 other normal-tension glaucoma patients who did not take **Methylcobalamin** supplements.⁵⁰ While 59% of the people not taking **Methylcobalamin** experienced worsening sight, **86% of patients taking Methylcobalamin experienced no loss of function.**

The Squeezing Spine

Lumbar spinal stenosis is the compression of the nerves in the lower spine caused by arthritis, spinal

lower back or buttocks, which is relieved by shifting position. In a single-blind, randomized controlled trial,⁵¹ 152 people with lumbar spinal stenosis were given the current standard care (physiotherapy, standard drugs, and education on managing their disease), and additionally either did or did not take **Methylcobalamin**. For whatever reason, the dose chosen for the trial was very low (half a milligram) compared to what has been used successfully in most trials pitting **Methylcobalamin** against nerve disease. At this low dose, there was no improvement in pain or in the doctors’ evaluations of the appearance, sensation, or function of their nerves; however, despite the clearly inadequate dose, those **people who took Methylcobalamin found themselves able to walk further distances without experiencing pains** than people who were not taking it.

Tinnitus

Just as the reception on your radio can be spoiled by nearby wires which aren’t adequately insulated, so the presence of nerves which aren’t properly insulated can create a sort of neurological “interference.” Many scientists believe that it’s just this sort of resonating interference which leads to the ringing of the ears in tinnitus. If that’s true, then **Methylcobalamin** – which in animal studies has been shown to help restore the nerves’ protective myelin sheaths, and whose deficiency leads to the loss of myelin – would seem like good candidate for a trial in folks with tinnitus.

Unfortunately, no such trial has been run. However, one study some years ago

did look at the effects of *conventional* B₁₂ supplements in people with both tinnitus and low serum cobalamin. **These patients**

experienced significant improvements in how loud the ringing in their ears sounded and in their overall perception of their tinnitus, though several other *specific* symptoms were not changed.⁵² It’s a good guess that the benefits these people experienced were due to the conversion of some of their B₁₂ to **Methylcobalamin**. If that’s so, then **Methylcobalamin itself** could emerge as a highly safe and potentially quite effective way to help restore proper hearing function in people with tinnitus.

Let There Be Light ... And Dark

Jet lag – the cloud of insomnia, lethargy, and mental fog which is associated, to varying degrees, with crossing time zones – is a good example of what happens when your body’s internal day-night clocks (**circadian rhythms**) don’t match up with the external cues of the world around you. Some people – folks on shift work, or who have **Delayed Sleep Phase Syndrome (DSPS)** or **Hypernycthemeral Syndrome** (a non-24-h sleep-wake cycle) – spend much of their lives walking through this haze. It may sound a little trivial to jump from **Methylcobalamin’s** powerful results in advanced neurodegenerative diseases to how it’s been found helpful in getting a good night’s sleep. But so many people do have real loss of quality of life from circadian rhythm disorders, and there has been *so much* research on **Methylcobalamin’s** ability to bring peoples’ circadian rhythms back in synch, that it would be leaving out a big part of the **Methylcobalamin** story if we didn’t at least mention it. Scientific journals abound with clinical trials⁵³⁻⁵⁸ demonstrating that **, thereby improving sleep quality and enhancing mental alertness.**

In fact, when Dr. Peter J. D’Adamo, author of the bestselling *Eat Right 4 Your Type*, discusses **Methylcobalamin** in his latest book,⁵⁹ he focuses almost entirely on the use of the supplement as a recipe for restoring these rhythms, never mentioning **Methylcobalamin’s** powerful neuroregen-



Methylcobalamin puts people back on track with their **circadian rhythms.**

degeneration, injury, or sometimes unfortunate genes. The squeezing of the nerves leads to pain on exertion in the



erative properties. “The gentlest and most effective way to phase-shift human circadian rhythm is using a combination of bright light exposure and methylcobalamin. Basically, methylcobalamin helps bright light do its job. Methylcobalamin also improves the quality of your sleep and helps you feel refreshed upon waking.” Dr. D’Adamo also notes that “Although methylcobalamin does not impact total levels of cortisol, it can help shift the peak of cortisol excretion, helping place your cortisol clock back on schedule” (cf. p. 246, where Dr. D’Adamo recommends **Methylcobalamin** for chronic fatigue syndrome).



How does it work? As Dr. D’Adamo points out, one major reason is that **Methylcobalamin makes the part of the brain which adjusts the body’s internal clocks more sensitive to light**.⁶⁰ In other words, it makes the message “Wake up! It’s daytime now!” come through more clearly. This, in turn, brings the body’s release of the “sleep hormone” **melatonin** back in line with the cycle of the day.^{61,62} Other circadian cycles – like peaks and valleys in levels of the hormone **cortisol**⁶⁶ and the changes in body temperature⁶³ – are also brought back in line by **Methylcobalamin**.

Yet light sensitivity can’t be the whole story. For one thing, Japanese scientists have reported a single case which, if confirmed by other investigators, would show that **Methylcobalamin restores the daily sleep-wake cycle in people who are totally blind**.⁶⁴ As well, the **body’s nighttime production of melatonin is actually less sensitive to being disrupted by brief exposure to light in the middle**

of the night in people taking **Methylcobalamin**.⁶⁵

Methylcobalamin is for Every Body!

With so much research backing its use in serious diseases of the brain and nervous system, it’s no wonder that many people suffering with such disorders are giving **Methylcobalamin** a second look. But even nerves which are in perfect health need **Methylcobalamin** for their normal functioning. It may be worth your while to ask yourself if it’s worth risking the loss of that health to a deficiency of this amazing coenzyme, when **new supplements which contain Methylcobalamin itself (and not just vitamin B12) are available**.

It’s important to know that, while some formulas contain **Methylcobalamin** in a form which is designed to be swallowed, these forms deliver nearly no **Methylcobalamin** as such to the brain and nervous system. Taking **Methylcobalamin** in a swallowed pill raises the level of this coenzyme in the liver, which can be useful for detoxifying the deadly amino acid **homocysteine**; but if you’re looking to get the neurological B12 to your **nerve cells, you’ll want to use a sublingual tablet**, so as to fortify them with the maximum amount of intact **Methylcobalamin**.

The body is a wonder, which amazes us with the feats of grace and beauty which it can perform, but without the brain and nerves to guide it, the body becomes a limp rag. Locked in the brain are the mysteries of what make us who we are. Ask yourself: will you wait for the Captain of the ship to stumble before you give her your support at the wheel?

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