Dementia? Schizophrenia? Parkinsonism? Could It Be B12?

B12 deficiency turns out to be much more common than statistics indicate, and it can have kind of serious consequences. It has been associated with or can actually cause premature aging and neurological disorders that are similar in presentation to dementia, multiple sclerosis or even Parkinson's. Conventional serum B12 tests, if you're lucky enough to ever be offered one, pick up only a small fraction of people who are actually B12 deficient and then only in the more advanced "stages" -- where the damage caused can be more difficult to "undo."

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What do all the following have in common?

- Cognitive decline, including conditions commonly labeled dementia and Alzheimer's
- Multiple sclerosis, Parkinson's and other neurological disorders
- Depression, anxiety, schizophrenia and other mental disorders
- Diabetic neuropathy
- Cardiovascular disease
- Learning or developmental disorders in kids, including autism spectrum disorder
- Autoimmune conditions
- Age-related macular degeneration
- Osteoporosis
- Male and female infertility
- Hyperpigmentation of the skin

Answer: They can all mimic the signs and symptoms of vitamin B12 deficiency.

After seeing three folks recently with scary, life limiting conditions (tremor with gait disturbance, feelingless feet with depression and even suicidal ideation, cognitive decline with osteoporosis and muscle wasting) in whom I suspected a nutritional deficiency explanation, I decided it was time to write about this.

Data from a Tufts University study suggests that 40 percent of people between the ages of 26 and 83 have plasma B12 levels in the low normal range—a range at which many experience neurological symptoms. Nine percent had an outright deficiency, and 16 percent exhibited “near deficiency.” Most surprising to the researchers was the fact that low B12 levels were as common in younger people as they were in the elderly.

This type of deficiency has been estimated to affect about 40 percent of people over 60 years of age. It’s entirely possible that at least some of the symptoms we attribute to “normal aging," such as memory loss, cognitive decline, and decreased mobility, are at least in part caused by a deficiency of vitamin B12.

I tend to get my most cutting edge diagnostic and treatment information from a handful of super smart folks (at least I find them super smart) who gravitate toward what is clumsily labeled functional medicine: Great Plains Labs’ William Shaw & Kurt Woeller, Chris Kresser of the eponymous Kresser Institute, and more lately James Greenblatt, an integrative psychiatrist based in Waltham, Mass. Most of what follows is kind of a mash up of their ideas/experiences with perhaps a bit of Kelly Brogan and Sarah Gottfried subconsciously melded in.

Common B12 Deficiency Symptoms

The signs of B12 deficiency can look like the symptoms of several other serious conditions. And the neurological effects of low B12 can be especially troubling.

Here are some of the most common B12 deficiency symptoms:

- Tingling or numbness of hands and/or feet
- Brain fog, confusion, memory problems, general cognitive decline
- Depression, anxiety, psychosis
- Anemia, weakness, fatigue
- Reduced appetite, weight loss
- Balance issues

Why Is It So Common?

B12 deficiency is significantly underdiagnosed for two reasons. First, it’s not routinely tested by most physicians. Second, the low end of the laboratory reference range is too low. It is well-established in the scientific literature that people with B12 levels between 200 pg/mL and 350 pg/mL -- levels considered “normal” in the U.S. -- have clear vitamin deficiency symptoms. In Japan and Europe, the lower limit for B12 is between 500 and 550 pg/mL. Some experts have speculated that the acceptance of higher levels as normal in Japan and the willingness to treat levels considered “normal” in the U.S. might even explain the low rates of Alzheimer’s and dementia in that country. Experts who specialize in the diagnosis and treatment of vitamin B12 deficiency suggest treating all patients that are symptomatic and have levels less than 450

pg/mL. They also recommend treating patients who show normal B12 levels but also have elevated urinary methylmalonic acid (MMA), homocysteine, or holotranscobalamin, which are indirect but sometimes more reliable markers of a deficiency in vitamin B12.

Apart from low dietary intake, the next (and in the elderly and folks with chronic GI problems possibly the biggest) culprit is absorption. Dietary B12 requires sufficient stomach acid to free it from its conjugated protein and then sufficient intrinsic factor for intestinal absorption. So anything that interferes with these steps can lead to low levels over time.

The final and also often overlooked cause is the use of nitrous oxide, as inhaled anesthesia. Again, especially in someone who's kind of borderline low to begin with, an otherwise routine dental procedure or relatively simple operation that requires general anesthesia could tip somebody into more serious deficiency. But the elderly and infirm are not the only ones at risk. Here's an intriguing case report from the Baylor University Medical Center of a 22 year old man who was using nitrous oxide recreationally. I remember we used to call them whippets:

> A 22-year-old man presented with a 1-month history of worsening hand numbness and difficulty with fine motor movements, followed by intermittent numbness in both feet and significant gait ataxia. He admitted to daily nitrous oxide abuse for months prior, reportedly inhaling over 30 whipped cream chargers daily. Serologic workup found his vitamin B12 level to be at the low end of normal at 222 pg/mL; however, his homocysteine and methylmalonic acid (MMA) levels were elevated at 16.3 µmol/L and 1.56 µmol/L, respectively. B12 supplementation was started along with cessation of nitrous oxide use, resulting in significant clinical improvement. The patient was not tested for other causes of B12 deficiency, such as atrophic gastritis, given his excessive use of nitrous oxide and improvement after discontinuation of nitrous oxide.

There aren't many studies (apart from those of the nucleoside era) of B12 levels in HIV+s. The only recent-ish one I could find was from Kampala (Uganda) and found that 36.8% of HIV+s (ambulatory, not on ART) had serum B12 levels less than 300 pg/ml. There was no comparator group, however, to see if this might simply be the case in the Kampala population generally. Interestingly, they found an "irritable mood" to be something of a marker for B12 deficiency. The authors note that similar surveys conducted (although in the '90s and early '00s) in Baltimore, Houston and Montreal have reported low or sub-optimal B12 levels in 12%, 13% and 30%, respectively (the Montreal group, as is common in Europe, used a cut-off equivalent to about 400 pg/ml whereas the other two used 163 and 211 pg/ml), which is unlikely to differ from the general population.

Who Is Most At Risk?

- Vegetarians and vegans
- Those aged 60 and over
- Those who regularly use acid-suppressing drugs

- Those on diabetes drugs like metformin
- People with Crohn's disease, ulcerative colitis, celiac, or IBS
- Women with a history of infertility and miscarriage
- Those with a history of nitrous oxide use, either recreationally or as a component of general anaesthesia

Even the New England Journal of Medicine and Harvard Medical School have been sounding the alarm lately, with this little blurb warning how "sneaky" the problem can be:

> "Over the course of two months, a 62-year-old man developed numbness and a pins and needles sensation in his hands, had trouble walking, experienced severe joint pain, began turning yellow, and became progressively short of breath. The cause turned out to be a lack of vitamin B12. It could have been worse. Severe vitamin B12 deficiency can lead to deep depression, paranoia and delusions, memory loss, incontinence, loss of taste and smell, and more."

What To Look For In Lab Work

Homocysteine is a marker that you shouldn't have any trouble getting your PCP to order. It's well known, it's recognized as a marker for cardiovascular disease, and it's pretty cheap. If you request a serum homocysteine, that's probably a good starting place. It's in indirect, inverse marker for some of the B vitamins, so a high homocysteine could be an indication of low levels of some of these crucial B vitamins. A high homocysteine doesn't necessarily mean you're deficient in B12, but especially if you have symptoms that could possibly have low B12 as their cause, it might be enough ammunition to then get your clinician to order some of the more advanced testing, like serum or urine methylmalonic acid. Folks who really know more about this than I do say thatmeasuring urine methylmalonic acid is better than measuring serum. And if you live in Europe or Japan, you also might be able to get a holotranscobalamin, or "holoTC," which is the most sensitive marker for B12 currently. If you can't get your doctor to order those tests, you can order some of these tests yourself from a growing number of DIY labs, but there is a bit of nuance to interpreting these tests, so it can be helpful to have somebody who is experienced in interpreting these tests working with you!

Since Lab Corp and Quest type reference ranges are designed to detect frank disease rather than an optimal level, getting a B12 tests back with a level of, say 250 or 300, is likely to be marked as normal, but at that level there's a really good chance that you are in the earlier stages of B12 deficiency, and then if you were to measure homocysteine or MMA, that those would be out of range as well. With homocysteine, the "upper limit of normal" typically goes up to 13, 14, or even 15 in some cases, but there's a considerable amount of research suggesting that once homocysteine levels start getting higher than 8 you probably want to make sure your folate (B9), B6 and B12 levels are okay.

The Four Stages of B12 Deficiency

B12 deficiency has been broken down by some into four stages, beginning with declining blood levels of the vitamin (stage I), progressing to low cellular concentrations of the vitamin (stage II), an increased blood level of homocysteine and a decreased rate of DNA synthesis (stage III), and finally, macrocytic anemia (stage IV).

The Problem with Conventional Serum B12 Testing

The conventional serum B12 (if you're ever lucky enough to be offered it) doesn't typically go out of range until stage three or four, so you're missing people in stage one or two if that's the only marker that's used. Homocysteine and methylmalonic acid can detect people in stage two deficiency. Holotranscobalamin or holoTC is the only marker, unfortunately, that can detect people in stage one deficiency. It's in a few teaching hospitals—Mayo Clinic, Cleveland Clinic and a few others—but you can't get it at your typical lab.

How to Treat a Deficiency

As always, adequate treatment depends on the underlying mechanism causing the problem. People with pernicious anemia or inflammatory gut disorders like Crohn's disease are likely to have impaired absorption for their entire lives and will likely require B12 injections indefinitely. This may also be true for those with a severe deficiency that's causing neurological symptoms.

Some recent studies have suggested that high-dose oral or nasal administration may be as effective as injections for those with B12 malabsorption problems. However, most B12 experts still recommend injections for people with pernicious anemia and an advanced deficiency involving neurological symptoms.

Assuming you don't have any of the stomach acid or gut problems mentioned above (which obviously need to be addressed), eating B12-rich foods is the preferred long-term solution. If you do eat animal products, B12 is richest in liver, clams, oysters, organ meats, and shellfish. If you were to eat a serving of liver and a serving of clams, oysters, or mussels even every other week, you would likely meet your B12 needs. Other seafood like fish eggs, octopus, crab, and lobster are also good sources for B12. Beef, lamb, (real) cheese and eggs are good sources of B12 as well, but they pale in comparison to organ meats and shellfish.

A common misunderstanding among many vegans and vegetarians is that it's possible to get B12 from plant sources like seaweed, fermented soy, spirulina, and Brewer's yeast, but many of those plant foods actually contain B12 analogues called cobamides that block the intake of and increase the need for true B12. If you are following a vegetarian or vegan diet, you should be definitely getting your B12 levels measured with the more sensitive markers mentioned above, and then supplementing with B12 if levels are out of optimal range.

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