**FOCUS:** As the former co-director of the Yale Multiple Sclerosis Program, you were at the forefront of one of the most prestigious institutions in the country. The research you have participated in has often involved participation in large clinical trials comparing different medications. And yet your approach to treating multiple sclerosis is surprisingly open and broad-based, including a willingness to consider off-label medications and nutritional supplements.

**GUARNACCIA:** I take an empirical approach to the treatment of multiple sclerosis, at the same time using therapies and approaches that have a solid scientific basis and conform to established principles in medicine. Sometimes that involves using drugs that are off label for multiple sclerosis, such as Rituximab, which is used in treating certain cancers and other autoimmune diseases. And sometimes that includes recommending nutritional supplements that have some scientific basis for their use. Of course, while we may not have Class I clinical trials supporting efficacy of various supplements, I endorse their use in patients who feel that this helps their symptoms and increases their quality of life. I consider this a reasonable approach.

**FOCUS:** Which supplements do you most commonly suggest for your patients?

**GUARNACCIA:** The newest supplement of interest is high-dose biotin, a B vitamin. As you know, promising new research suggests that biotin may be helpful in slowing or halting progression of both primary and secondary progressive multiple sclerosis in a subset of patients. I have seen a range of responses in my own patients, both those with primary and secondary MS, and those with relapsing-remitting MS. I have seen improvements in energy, cognition, and overall feelings of well-being. Some patients report an improvement in ambulation and motor strength, or better bladder control. Like many prescription and nonprescription treatments, there is a range of responses. I take high dose biotin myself though I don’t have MS, and feel a subtle benefit. The scientific basis for biotin relates to its role in energy metabolism and myelin formation.

**FOCUS:** The research thus far has focused on patients with primary or secondary progressive MS. Have you found it helpful for relapsing/remitting MS as well?

**GUARNACCIA:** Yes, but I don’t think there is an absolute division between the two. I have patients who are on the very mild end of the scale with relapsing/remitting MS and have almost no functional limitations but still suffer symptoms such as fatigue, pain, bladder control issues and cognitive dysfunction that significantly impact their lives, who potentially may respond to high dose biotin. Studies have shown that loss of neurons can occur very early in multiple sclerosis and we do not have any FDA-approved treatments that focus specifically on neuroprotection.

**FOCUS:** What other supplements do you recommend?

**GUARNACCIA:** Like many specialists in multiple sclerosis, I stress vitamin D in my practice. Low vitamin D levels are clearly associated with risk of developing multiple sclerosis and there is some data that shows that higher vitamin D levels may impact inflammation and the course of the condition. I also routinely check vitamin B12 levels and find that vitamin B12 supplementation not infrequently improves fatigue. We often must resort to off label...
prescription medications to treat MS fatigue because there are no on label treatments; the problem is that these medications are often costly and the process of getting insurance coverage is frequently difficult.

Most if not all my colleagues are recommending vitamin D supplementation. Research has shown that MS risk is linked to low vitamin D levels, and there is some evidence that patients with higher levels do better in terms of relapse rates.5-6 Besides, low vitamin D is linked to several other illnesses, including cardiac disease,7 depression8 and colon cancer.9

FOCUS: Do you feel there is an emerging synergy for MS patients of nutrition, supplementation and medication?

GUARNACCIA: With supplements like biotin coming to the fore, with support from scientific studies and with an increasing emphasis and research on the significance of dietary changes, I do think there’s a dimension to MS that can impact patients’ quality of life. Recently the Wahls diet has gained renown, and I think for motivated patients, diet can make a difference. I have patients who avoid gluten, or patients, diet can make a difference. I have patients who avoid gluten, or patients, diet can make a difference.

I have seen a range of positive responses to biotin in my own patients, both those with primary and secondary MS, and those with relapsing-remitting MS.

Key Papers by Dr. Guarnaccia


References


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Dr. Guarnaccia is co-founder, with pharmacist Annmarie T. Arvanites, of Metabiome LLC.
New Technique Neutralizes Biotin Interference in Laboratory Tests

High-dose biotin therapy has been shown to be beneficial in progressive multiple sclerosis (MS) and is expected to be adopted by a large number of patients, according to a new research paper published February, 2017 in Clinical Chemistry and Laboratory Medicine. In 2016, Harvard Medical School researchers reported three cases of high dose biotin interference in laboratory tests, and wrote: “We anticipate more cases of biotin interference. In the month these cases were being reviewed, a local compounding pharmacy dispensed 370 one-month prescriptions of high dose biotin (personal communication).” Biotin therapy can lead to interference in many immunoassays that utilize streptavidin-biotin capture techniques. This can lead to falsely high results in competitive assays (usually small molecules such as steroid or thyroid hormones) and falsely low values with the so-called sandwich assays (for example peptide hormones).

The most frequently reported cases are false diagnoses of hyperthyroidism. Moreover, if a patient does not report the fact they are taking a biotin supplement, or if their treating physician is unaware of the potential interference with certain tests, incorrect test results can lead to further evaluation and even initiation of inappropriate treatment with possible adverse effects.

One recommended approach has been a simple biotin washout period of up to 2 weeks (see FOCUS, August 2016, “A Paradigm Shift in the Treatment of Progressive Multiple Sclerosis”). However, if a patient does not have awareness of this or does not anticipate the test will be drawn they are unable to appropriately prepare and incorrect results may be reported.

Now, a new paper reports that a simple method to remove biotin from laboratory samples can be easily implemented and is unlikely to affect any current assay methods. The technique efficiently removes biotin even at the highest concentrations. Twenty-seven samples from 20 MS patients receiving various high doses of biotin were studied. The “neutralization protocol” was applied to the samples from individuals both on high dose biotin, and those not taking the supplement. (Note: The amount of biotin that may interfere is variable across tests. Some have an interference threshold at about 100 ng/mL of plasma biotin (meaning that below 100 ng/mL the results are not biased, and above 100 ng/mL results are biased), while the threshold can be as low as 5 ng/mL for other tests.) The neutralization technique effectively removed excess biotin but did not affect samples from patients not on the supplement. The researchers report that their method “can be widely implemented and is unlikely to affect any of the current assay methods.”

Biologist Marie Piketty, one of the study authors, discussed the method with FOCUS: “To overcome this biological interference, we have recently proposed a simple method which can be easily implemented in any laboratory. This method uses a commercially available reagent (streptavidin micro particles) and takes approximately 1.5 hours. It may be undertaken in any patient identified as being treated with biotin (highlighting the importance of the information provided by the clinician to the clinical chemist about the treatment taken by its patients) or when a biological presentation of an endocrine disorder is found in an asymptomatic patient. This method is currently an in-house method (i.e. all labs must do this by themselves) and may be considered to be a little bit time-consuming by laboratories that run thousands of tests each day. We expect however that immunoassay manufacturers will introduce an automated method in their machine to detect and remove this biological interference. Finally, it must be noted that, in our above-mentioned study, we used reagents from Roche Diagnostics, a European manufacturer that extensively uses the streptavidin-biotin methodology to separate bound and free antigen. However, many other manufacturers use the same methodology, and we expect that we and other researchers will test whether our method is also applicable to these reagents.”

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