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*AACC Guidance Document on Biotin Interference in Laboratory Tests.*

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**Guest:** Dr. Mark Cervinski is an associate professor of Pathology and Laboratory Medicine at the Geisel School of Medicine at Dartmouth and director of clinical chemistry at Dartmouth-Hitchcock Medical Center in Lebanon, New Hampshire.

Randye Kaye:

Hello and welcome to this edition of JALM Talk, from *The Journal of Applied Laboratory Medicine*, a publication of the American Association for Clinical Chemistry. I'm your host, Randye Kaye.

Biotin, also known as vitamin B7, is a coenzyme required for many metabolic processes. Biotin may be used for therapeutic purposes such as in the context of multiple sclerosis and it is also marketed in over-the-counter multivitamins for cosmetic purposes such as for hair, nail, and skin health. Biotin is also an essential reagent in many laboratory tests, particularly in immunoassays that use biotin and streptavidin binding.

In 2017, the Food and Drug Administration warned that high levels of biotin in laboratory samples may interfere with certain tests and cause incorrect test results. This FDA warning combined with related case reports has many laboratorians and clinicians wondering how to deal with the potential for biotin interference. The AACC Academy of distinguished laboratory experts developed a document intended to provide guidance to laboratorians and clinicians for preventing and identifying biotin interference. This guidance document was published as a special report in the May 2020 issue of *The Journal of Applied Laboratory Medicine*.

An author on this report is Dr. Mark Cervinski. Dr. Cervinski is an associate professor of Pathology and Laboratory Medicine at the Geisel School of Medicine at Dartmouth and director of clinical chemistry at Dartmouth-Hitchcock Medical Center in Lebanon, New Hampshire. Dr. Cervinski is our guest for this podcast. Dr. Cervinski, what is biotin? What is it used for and why all the hype around it recently?

Mark Cervinski:

All right. So, biotin is a water-soluble vitamin that our bodies use as a coenzyme for a large number of different enzymatic reactions in our bodies that our metabolism uses to maintain normal health. The hype around biotin really centers around the recent marketing of high doses of biotin to improve hair and nail texture and largely are seen as a supplement to enhance the appearance of hair and nails.

Now the hype in some of the lab community comes from the fact that these high doses of biotin can cause interferences for some of the tests that we do in many clinical laboratories.

Randye Kaye: Oh, so how exactly does it interfere with lab tests and with what types of lab tests?

Mark Cervinski: Well first, I think it's important to know that biotin will only affect immunoassays. So, these are tests that use an antibody to recognize a specific component of a patient sample. These antibody antigen interactions can be affected on some manufacturers' tests because the antibody, or the antigen, depending on the assay format, could be labeled with biotin. And biotin will bind with really really high strength, or affinity is the term we use, to streptavidin. And so the pair, the streptavidin and biotin pair, can be used to pull down these immune complexes so that we can measure different hormones like thyroid stimulating hormone or HCG which is the hormone we monitor for pregnancy.

Randye Kaye: If interference is a potential issue as you say, then why are biotin and streptavidin commonly used in laboratory tests?

Mark Cervinski: The reason why biotin and streptavidin are commonly used ties back into the issue of biotin and streptavidin having very, very high affinity for one another. In fact, it's one of the strongest known binding affinities in nature that is not a covalent bond. So, these things aren't permanently bound and they can fall apart from each other but it's a really, really strong tight bond. So that makes it a really efficient tool for us to pull down these immuno complexes out of solution and it makes for an automated immunoassay that can be conducted very quickly in a high-throughput laboratory. So, it generally hasn't been a problem for the laboratory because the concentration of biotin that we normally have in our serum has been historically lower, and that's because we were getting our biotin from our normal diet. But these higher concentrations of biotin that we are now starting to see from those who are taking biotin for hair and nail supplementation can produce an interference in these assays.

Randye Kaye: Yeah, the body's balance is very finely tuned. What led the AACC to develop a guidance document on biotin interference and laboratory tests?

Mark Cervinski: Well, we noticed that there were a lot of publications over the last few years that have come out, both case reports and studies in which investigators have spiked in biotin into different samples. And given that there were so many different areas of publication, we felt that one of the best ways to serve our laboratory community would be to take all

these different resources and pool them into one document that can become a de facto reference document for the laboratory community.

- Randye Kaye: Can you briefly describe some of the major findings from the report?
- Mark Cervinski: Sure. So, one of the things about this report is that since it is effectively a guidance document, there wasn't a lot of new fact-finding here. But we were able to summarize into a cohesive message in this report are some recommendations that the laboratory can use to mediate or manage this biotin-mediated interference. So, one, thankfully, biotin is a water-soluble vitamin that's quickly cleared from our bodies. It has a half-life of about two hours. So, even if someone were taking a larger dose of over-the-counter strength biotin, which is anywhere between 5 and 10 mg a day, waiting for as little as 8 hours is enough time to let all that excess biotin be flushed from the body. Now, if the patient's been taking a higher dose such as those that may be seen in patients who are being treated for multiple sclerosis, it may take up to 72 hours for the biotin to reach a low enough concentration to avoid some of this interference.
- Randye Kaye: Well, how often do patients present with biotin in the concentration range that may result in interference?
- Mark Cervinski: Yeah. That's a great question. And really, we don't have solid data from all across the country and I'm sure the percentages are changing over time as the fad ebbed and waned. But what we know from one study at the Mayo Clinic is that, around 7% of the population that came into the ED, to the emergency department that is, had high enough concentrations to produce interference in some tests. Now, the concentration needed to interfere with one test versus another test on the same manufacturer's platform versus different manufacturers can vary but at a threshold that they predetermined, it was about 7% of the population.
- Randye Kaye: Wow. So, finally, what recommendations do you have for laboratories who are concerned about the potential for biotin interference with their assays?
- Mark Cervinski: Well, the first thing for the laboratory is to review the test that you have in your menu and see which ones have the potential for being interfered with by higher concentrations of biotin. I also think that it's really crucial for laboratory professionals to get out of the laboratory and do a little bit of communication about this issue. Speaking from my own experience at my institution here, we are frequent contributors to the endocrine case conference and our

endocrine colleagues are certainly some of the biggest users of these immunoassay tests. And more than once, I can say that either I or one of the other clinical chemists here have been called upon to describe biotin-mediated interference to the attendees of that conference.

So, I think that education and communication with clinical providers is key to make people aware of this issue. Now, if you have a sample that you have suspicion for biotin-mediated interference, there are a couple of things that the laboratory can do. One, if you're fortunate enough to have another method in your building that doesn't use the biotin-streptavidin pair, you could test that sample on that test or you can send it to another laboratory in your town if they use a method that is not subject to this interference.

And then finally, there are now some third-party reagents on the market that can effectively pull the biotin out of the sample before it is being tested, but of course, it would become cost-prohibitive to pretreat every patient sample before it's tested. So, the challenge really is trying to figure out which of these samples has biotin-mediated interference. And for us to know that, we really need to have a strong working relationship with our clinical colleagues. They need to be the ones to identify to us that, "hey, you know, these results don't really match up with what I would expect for this patient. Is there a possibility that there's an interference with this test?"

Randye Kaye: Very interesting. So, as always, communication is key. Thank you for joining us today, Dr. Cervinski.

Dr. Mark Cervinski: Oh, thank you very much Randye. It's been a pleasure.

Randye Kaye: That was Dr. Mark Cervinski from Dartmouth-Hitchcock Medical Center describing the JALM Special Report, "AACC Guidance Document on Biotin Interference in Laboratory Tests." Thanks for tuning in to this episode of JALM Talk. See you next time. And don't forget to submit something for us to talk about.