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Bad Tests Die Slowly: The Myelin Basic Protein Example.
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Guest: Dr. Lisa Johnson is a medical director in clinical chemistry at ARUP Laboratories and an assistant professor in the Department of Pathology at the University of Utah.

Bob Barrett: 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 am your host Bob Barrett, sitting in for Randye Kaye.

Multiple sclerosis, or MS, is a debilitating disease of the central nervous system that can be difficult to diagnose. A diagnostic workup for MS may include a combination of clinical examination, imaging, and laboratory tests. In particular, analysis of the cerebrospinal fluid, or CSF, may be helpful when imaging findings are inconclusive.

However, some CSF tests are better than others. A Focused Report published in the January 2020 issue of *The Journal of Applied Laboratory Medicine* describes efforts by a national reference laboratory to improve the utilization of CSF tests for MS. Specifically, the authors sought to decrease the use of the myelin basic protein test in favor of the oligoclonal bands test, which has greater specificity for MS. Interventions included educational efforts as well as the removal of the myelin basic protein test from a multiple sclerosis panel offering.

The first author of the report is Dr. Lisa Johnson. Dr. Johnson is a medical director in clinical chemistry at ARUP Laboratories and an assistant professor in the Department of Pathology at the University of Utah. She is our guest in this podcast today.

So Dr. Johnson, a few questions to start out. Can you briefly describe the two CSF tests for which you compared ordering behaviors, myelin basic protein and oligoclonal bands? Which one is better for multiple sclerosis, and why?

Dr. Lisa Johnson: So myelin basic protein is basically a marker of neuroinflammation and oligoclonal bands is looking for different banding patterns of IgG in the CNS and so the one that's better for multiple sclerosis is the oligoclonal bands. It's more sensitive for multiple sclerosis.

Bob Barrett: So why do you think the clinicians continue to order myelin basic protein for patients suspected to have multiple sclerosis?

Dr. Lisa Johnson: So we currently do not understand the exact pathological mechanism for multiple sclerosis. We know that it is a chronic inflammatory demyelinating disease that involves the immune system and the central nervous system; however, we are still trying to tease out the specific mechanism, which is probably complex.

In the past, several studies have proposed a role for antibodies against NBP in the pathogenesis of MS. So the theory was that antibodies were targeting NBP and if we stop these antibodies, then we could potentially treat MS. And these studies are published in very prominent journals. Unfortunately, the mechanism doesn't appear to be that simple, and more studies have come out to show that antibodies against NBP are non-specific and probably not a driver of the disease.

Since NBP is a major component of the myelin sheath, it is likely a bystander protein that indicates that damage or inflammation occurred in the CNS.

So NBP is part of the history in searching for the mechanism of MS, which is maybe why clinicians still think of ordering it when working up a patient for multiple sclerosis.

Bob Barrett: So doctor, what prompted your team to retrospectively review the utilization of multiple sclerosis testing?

Dr. Lisa Johnson: So, Dina Greene and Bob Schmidt as well as David Grenache had performed a study in 2012 that found that myelin basic protein results were neither sensitive nor specific for the diagnosis of multiple sclerosis.

So they further analyzed the concordance of NBP, the “bad” test, with the “good” test, oligoclonal bands, and saw that the concordance rate was about 67%, so it wasn’t great.

Additionally, the newest revisions of the McDonald criteria came out in 2017, and one point that the authors of the McDonald criteria, which are the diagnostic criteria for multiple sclerosis, stressed, is that it's important to judiciously rule out other diseases before making the diagnosis of MS.

And so the authors mentioned that it's important to think about the sensitivity and specificity of different testing when ruling in or ruling out a diagnosis of MS. And since NBP is neither sensitive nor specific, this is consistent with the ideas put forward in the guidelines.

So therefore, we wanted to do a retrospective analysis to see how the publication in 2012 and removal of NBP from the panel of MS testing possibly affected orders for NBP.

Bob Barrett: In your mind, what do you think were the most important findings of the review?

Dr. Lisa Johnson: So the most important finding of the review is that we did see a decrease in utilization of NBP testing since 2012. And so we do see that the orders for the testing are decreasing, but probably not as much as we would like.

And so this is kind of a sign to us that we did these utilization efforts, we removed NBP from the panel, and we published a publication that stated that it was not sensitive nor specific for MS, but these were more gentle approaches. And so, if we want stronger results we probably have to take harsher action.

Bob Barrett: Well finally Dr. Johnson, what are some of the benefits and challenges that clinical laboratories face in participating in test utilization efforts?

Dr. Lisa Johnson: I think that the biggest benefit that the laboratory has is that they have all the data and they have the people and the tools to analyze the data. The challenge is, is that we need to somehow get this data and information out to the ordering providers.

And so, it's kind of interesting to think about, what are different strategies that we can use to do this? I think in the future, it will be important to publish more instances of these strategies so that people can learn what works and what doesn't work and what is most effective when doing these utilization efforts.

Bob Barrett: It's great information. Dr. Johnson, thank you so much.

Dr. Lisa Johnson: Okay, great!

Bob Barrett: That was Dr. Lisa Johnson from ARUP Laboratories and the University of Utah, describing her focused report from the January 2020 issue of JALM entitled, “Bad Tests Die Slowly: The Myelin Basic Protein Example.”

Thanks for tuning in to this episode of “JALM Talk.” Tune in next time and don't forget to submit something for us to talk about.