# Lab leaders on variant testing and result requests

**Plus, pre-procedure testing and more**

May 2021—*How variant testing is being handled and how labs should respond to clinicians' requests for the results was a topic of discussion when Compass Group members met April 6 with CAP TODAY publisher Bob McGonnagle for their monthly roundtable on COVID-19.*

*The group's members provided a follow-up on post-vaccination infections and reports on pre-procedure testing, and their thoughts on whether the focus has shifted away from testing amid the press to vaccinate. Until it's known whether the U.S. can keep pace with vaccination alone, "it's a mistake to take our eye off of what testing can offer, especially in terms of variant detection," said Sterling Bennett, MD, MS, of Intermountain Healthcare.*

*Answering McGonnagle's questions, in addition to Dr. Bennett, were Stan Schofield, MaineHealth; Terrence Dolan, MD, Regional Medical Laboratory; Steven Carroll, MD, PhD, Medical University of South Carolina; Janet Durham, MD, ACL Laboratories; Andy Drury, OhioHealth; Linda Mirkes, MBA, MT(ASCP), Atrium; John Waugh, MS, MT(ASCP), Henry Ford; Joseph Baker and Peter Dysert, MD, Baylor Scott & White; Darlene Cloutier, MSM, MT(ASCP), HP, Baystate; Judy Lyzak, MD, MBA, Alverno; Jennifer Laudadio, MD, University of Arkansas for Medical Sciences; Greg Sossaman, MD, Ochsner; and Walter Henricks, MD, Cleveland Clinic.*

*The Compass Group is an organization of not-for-profit IDN system lab leaders who collaborate to identify and share best practices and strategies. Here's what they had to say.*

**In our last call in early March, a few of you said you were collecting cases of people who had become infected post-full vaccination and hoping to understand whether the cases might be related to variants. Stan, would you like to be the first to comment on where we stand with variants or people becoming infected after full vaccination?**

*Stan Schofield, president, NorDx, and senior VP, MaineHealth:* We have variants here, but they're from people who have not been vaccinated. Eighteen care team members in the health system in the past four weeks tested positive for COVID after the second vaccination, but none of them is confirmed as a variant. We sent a number of them off to sequence, but they were not sequenced as a variant. We're starting to see U.K. B.1.1.7 because we're testing for that now. When the ID doctors get the results, we'll reflex and do the variant determination.

**Terry Dolan, what has been your experience in Tulsa so far with patients showing infection after full vaccination or patients who are turning up with variants?**

Dr. Dolan

*Terrence Dolan, MD, president, Regional Medical Laboratory, Tulsa, Okla.:* We're seeing variants like everyone else. We have several patients who became infected with COVID after the first immunization. We are doing a lot of antibody studies at this point in time, and we've found that those who have had relatively mild COVID infection in the past have antibody levels that are not that high, and that's why we recommend they be immunized. I've seen patients who become infected after the first immunization. We waited 90 days before giving them the second

immunization.

Going forward, we are looking at the capsid antibody and the spike antibody to give us insight into where a patient is immunologically. I believe antibody testing will be valuable in evaluating the immunologic status of the patient, especially immunocompromised patients. We have patients who've had both immunizations and their titers are low, suggesting that they may not be protected compared to other patients with very high titers who may be protected. I would definitely titer anyone with an underlying disease. Which titer level is protective is still under investigation, but we have seen a very wide divergence in titers.

**Steve Carroll, you had spoken last month about trying to follow some of these cases. Do you have an update for us?**

*Steven Carroll, MD, PhD, chair, Department of Pathology and Laboratory Medicine, Medical University of South Carolina:* We have been following them, but our experience is similar to Stan's. We have had people who have turned up infected after getting vaccinated, but thus far none of them has had a variant. It's been more run-of-the-mill COVID. We have both the South African and U.K. variants here, but we still are not seeing that those are breaking out as the ones that are defeating the vaccine.

**Janet Durham, tell us what your recent experience has been and where you stand generally in this pandemic.**

*Janet Durham, MD, medical director, Wisconsin operations, ACL Laboratories, and president, Great Lakes Pathologists, West Allis, Wis.:* Wisconsin is pushing out the vaccines, and the health care system is taking a big part in that initiative. We have plenty of reagent for testing. Our test volume in the last three weeks has gone up about 12.7 percent, and our positivity rate—inpatient, ED, and outpatient—is also increasing, about 0.9 percent up from the week prior. As more people get vaccinated, it will be interesting to see where the test volumes go.

When we spoke in early March, our system was trying to determine how to handle pre-procedure testing, because a lot of patients had not been coming in for some of the procedures that were requiring quarantine. We didn't have enough of the rapid PCR testing to accommodate all of those locations. So the system has been trying to soften the quarantine requirements, still doing the testing ahead of the procedure but telling patients that as long as they're masking and staying socially distanced, they don't have to stay at home. We're trying to at least encourage patients to get their screening.

**Nationally we see increasing rates of positivity and I don't think anyone knows entirely whether this is due to social behavior—although the rates are going up in young people—or variants. Andrew Drury, what do you make of the recent reporting about the rates, both public and within health care?**

*Andy Drury, laboratory director, Riverside Methodist Hospital, OhioHealth:* It's concerning. Here in Ohio we saw a rapid decline from what our peak was in late November and early December, but within the past three weeks we've seen it plateau and start to rise. During the plateau our positivity rate was three to four percent; we're now in the six to eight percent positivity range. It hasn't been reflected in our volumes, which have remained flat throughout the past about 12 weeks. So we've hit a plateau in testing but our positivity rate is up. Currently we are seeing our highest positivity in patients below the age of 50.

**Linda Mirkes, what is your recent experience?**

*Linda Mirkes, MBA, MT(ASCP), assistant VP, core laboratory and integration, Atrium Health, Charlotte, NC:* Our positivity rate has been going down, but in the past couple of days we've seen a few ticks up. Our 30-day rolling is around four percent. The providers have started to ease some of the pre-procedure testing for low-risk procedures. We have plenty of reagent and capacity. We're finally at a point where we can do all our testing in-house. But we're watchful and careful and keeping our eye on everything.

**John Waugh, Michigan is a hotspot. Tell us what the latest is.**

*John Waugh, MS, MT(ASCP), system VP, pathology and laboratory medicine, Henry Ford Health System, Detroit:* Our positivity rate for the past 24 hours was 20.5 percent. We have been on a hot cycle, climbing up from about 2.5 to 3.5 percent about four weeks ago. The majority of new infections are typically people in the 20 to 60 age group. There has been pretty good uptake of vaccines here. We think what we're seeing are, first, viral variants. Second,

probably a fertile opportunity for infection due to previous low statewide infection rates during that time. And third, pandemic fatigue. We still have a good percentage of mask wearing and other precautions, but the numbers are dizzying right now. And just reported today: about 30 people who were previously vaccinated who tested positive, all with mild symptoms.

**Are you seeing a higher positivity rate in younger patients?**
*John Waugh (Henry Ford):* Yes, and these are people who had not qualified for vaccines until that point. They dropped the age to 16 statewide this week.

**Joe Baker, what is your experience in Dallas?**
*Joseph Baker, VP of laboratory, Baylor Scott & White Health, Dallas:* Our overall positivity rate has plateaued at about 4.1 percent. We've hung around that for the past five to six weeks, and our testing volume has remained steady too. The specific area we have seen an increase in is the 15 to 34 age range.

*Peter Dysert, MD, chief, Department of Pathology, Baylor Scott & White Health, Dallas:* We're also starting to see variants. Over the past two weeks, we've had 50 plus cases of *S* dropout, what we assume is the U.K. variant. We sent all of those to our state and are waiting on confirmation while we bring up our in-house sequencing capability using the state lab's results to help validate us. Our positivity rate now for hospital inpatients and pre-procedure testing is about 2.5 percent. When you add in the outpatients, it goes up to that four percent Joe mentioned.

**Are you happy with the state turnaround time or is the state overwhelmed?**
*Dr. Dysert (Baylor):* They're overwhelmed and they farmed out everything. They farmed out the bio pipeline piece. They sent things to the CDC. They're doing very little in-house.

**Darlene Cloutier, what's happening at Baystate?**
*Darlene Cloutier, MSM, MT(ASCP), HP, director of laboratory operations, Baystate Health, Springfield, Mass.:* In Massachusetts we're going in the wrong direction. We were planning some unwinding strategies at Baystate, getting de-escalation procedures together, and we have not been able to get that in place because our rates—Vermont, New Hampshire, Massachusetts, New York—are going up, from two percent in Massachusetts to a nine percent positivity rate. At Baystate we're at about five percent for the past 24 hours.

We have capacity and reagent. Our volumes started to increase a little over the past couple of weeks. We were trying to focus on returning to normal, but we're not there yet.

**Do you believe this increase is mostly behavioral?**
*Darlene Cloutier (Baystate):* I do. This past Sunday, Easter, I went for a walk around my neighborhood and saw a lot of cars and people gathered at houses. It was a little discouraging to see. The lines for vaccination in Massachusetts are long and it is not easy to get vaccinated now. People under the age of 55 are still waiting.

**Judy Lyzak, what are you seeing?**
*Judy Lyzak, MD, MBA, VP of medical affairs, Alverno Laboratories, Indiana and Illinois:* To quote one of my ID physicians, everybody's tired of COVID except for COVID. COVID is having a great time. On our incident command calls for our organization, our CMO is essentially telling us we are now in the fourth wave. We're seeing an increase in our symptomatic patient rate at all of our hospitals except three. The rate for the folks we're screening for surgery is now over one percent again. We were going in the right direction for a long time and now we're going in the wrong direction. Testing volumes are stable.

**What has been your experience so far with variants, and how are you dealing with them when you find them on screening?**
*Dr. Lyzak (Alverno):* In Illinois and Indiana we collaborate with the two respective public health departments, which have a convoluted way of dealing with this. Basically, if you as a clinician have a concern that your patient, due to vaccine breakthrough, reinfection, or travel history, for example, may have a high likelihood of a variant, you have to approach and get permission for sequencing from the state board of health. Once permission is granted, then the state board of health reaches out to the laboratory to procure that specimen. And they have certain criteria

and cutoffs or cycle times, et cetera. We've also collaborated with them on a surveillance program to send 10 specimens per week per state. We have a slightly different approach: Those results are opaque. They're not provided to the clinician for treatment, and we don't see that. I don't have a lot of experience with that because those results are essentially hidden and they're really for surveillance.

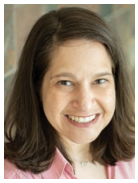
**So no real data back into the hands of people who might need it or want to use it for patient care?**
*Dr. Lyzak (Alverno):* That's right.

**Jennifer Laudadio, you're in Little Rock. I'm assuming the weather's nice, students are around, people are looking to have a good time. Do you see a concomitant rise in infection rates?**
*Jennifer Laudadio, MD, professor and chair, Department of Pathology, University of Arkansas for Medical Sciences College of Medicine:* We have not seen it yet. We're still at about two to four percent, which is our lowest level. But I am skeptical of the future. When this started in March 2020, we trailed the rest of the nation. It kind of started on the edges and worked its way inward to Arkansas. So what's happening in Detroit has caught my attention, and I imagine that in the next few weeks we will start to see those positive numbers increase.

**Tell me about your experience in dealing with the variants. And if you were in charge, how would you, as a molecular pathologist, want to see the country handle the COVID variants?**
*Dr. Laudadio (UAMS):* It's been challenging for us in Arkansas. We don't necessarily have the capacity to do surveillance testing in-house. We've had conversations with many companies and put together a proposal for our hospital administration. It's just a matter of them not wanting to invest the dollars at this point because they've spent so much money on COVID already, and I can understand that. So we're still using the health department for surveillance when we have patients who have been vaccinated and come up positive. Those are the targeted patients.

There are other assays where you don't have to do sequencing to detect certain variants. That is attractive, but at the same time, in listening to the news and to our colleagues, we know that the mutation rate is high and new variants are emerging. If you invest in a test that detects only four or five variants but it turns out that variant number six becomes clinically relevant, you're not going to have the capacity to detect it. So I think sequencing is the way to approach this.

One of the challenges for all of us is that if we're not doing this in a manner that returns patient-specific results to guide patient treatment, we're not dropping a charge. So we're truly doing it for surveillance and that's a different model for a clinical laboratory. We've partnered with some of our research lab friends who have gone through the IRB process. We're just starting to feed them samples to do testing here at UAMS. But the positive rate is so low now that we don't have much to give them.


Dr. Laudadio

**Do you think we just cannot reach the sequencing capacity we're going to need to deliver variant results directly back to labs and clinicians?**
*Dr. Laudadio (UAMS):* I think we can do it, and as a community of laboratory professionals, we'll find a way to do it just like we did with testing. But it's unfortunate that there is no strong, coordinated effort to increase capacity. Our state department of health contacted us to explore what our capacity could be, but there's been no dollars to support it and no coordinated effort to build that testing.

**Greg Sossaman, do you think perhaps, given the availability of vaccines, someone somewhere has**

**taken their eye off the testing ball, so to speak, particularly as it relates to the need for sequencing variants and trying to figure out what it's going to mean in patient populations?**
*Greg Sossaman, MD, system chairman and service line leader, pathology and laboratory medicine, Ochsner Health, New Orleans:* We've definitely seen that here. The attention as a health system toward testing has shifted toward vaccination. We were having calls every day with our ID colleagues, the testing teams, and I think we've lost some of that focus. We similarly have put forward a plan to bring in sequencing equipment to look for variants in our community and gotten nowhere with that request for capital.

We're also looking at a couple of other things and haven't seen the same degree of interest in testing. It seems to have moved on to vaccination. I suspect that at a state level we're seeing that same falloff in focus as they push toward vaccination with limited resources.

We have a program that is similar to what Dr. Lyzak described. If a physician needs to look for a variant, they have to talk to the state; then we will pull the specimen and send it. There's no automatic program for that and we're not doing it in-house. So, yes, it seems like the focus on testing has fallen off.

**Sterling Bennett, I know you keep an eye on the nation and these important policy decisions. Do you share this idea that perhaps we put too many chips in the vaccine boat and forgot about testing?**
*Sterling Bennett, MD, MS, medical director, Intermountain Healthcare central laboratory, Salt Lake City:* I can understand the shift in focus to vaccines. If you're tired of mucking out the stable, rather than find a better way to shovel manure, just stop feeding the cows. So I think the shift has been to stop feeding the cows through vaccination. It's a great strategy as long as it works, but the variants raise concern long term of whether we'll be able to keep pace with vaccination alone. Until that's been demonstrated, it's a mistake to take our eye off of what testing can offer, especially in terms of variant detection.

**Terry Dolan, what are your current procedures for pre-procedure testing? Has there been a shift in the recommendations and some easing of the stringency of testing pre-procedure?**
*Dr. Dolan (Regional Medical):* It depends on the hospital and medical staff. Some hospitals still are testing 100 percent of the presurgical patients—I think that's wise—and others are testing intermittently based on symptoms. Of course we all know a fair number of people are asymptomatic or positive. There may be more flexibility with GI procedures, such as colonoscopy, et cetera.

**And do you think there may be an excessive emphasis on vaccines perhaps at the expense of the kind of testing that might now be needed for variants or people who are becoming infected post-full vaccination?**
*Dr. Dolan (Regional Medical):* Even the best vaccines are in the low 90s, maybe up to 95 percent effective, and those that we've seen break through where there have been preliminary studies, they're relatively small. They're not up to the five to six or seven percent we would expect on the Moderna and Pfizer vaccines. We expect some to break through. As I mentioned, we're looking at those patients from an antibody standpoint, and we are finding some who have very low antibody who have been infected and have been vaccinated.

There hasn't been a lot of talk about antibodies, but I think we're going to be doing more and more of that because of the breakthroughs and so on. We need to be careful to avoid over-immunizing patients. There is a syndrome called immune paralysis that is a scary situation. You don't want to over-immunize because patients' immune systems may fail in that situation. If there is an extremely high titer, one may be reluctant to give them a second immunization.

*Stan Schofield (MaineHealth):* It's important to remember that 20 percent of the U.S. population doesn't want the vaccine. We're chasing the population to vaccinate, but there's a small core group that's always going to be problematic until they eventually become infected or are immune through herd immunity.

I think testing has suffered a little bit. It's not in the limelight. Our volumes are half of what they were but so too are the symptomatic patients. The asymptomatic population for us is still strong every day for presurgical and pre-procedure cases in all 12 of our facilities.

**Wally Henricks, what's going on in Cleveland? I'm sure you're seeing variants. You're probably trying to sequence them yourself; you have equipment for that.**
*Walter Henricks, MD, vice chair, Pathology and Laboratory Medicine Institute, and laboratory director, Cleveland Clinic:* We continue to test all pre-procedure patients across the board. Positivity rate is about 0.5 percent. Overall positivity rate is about 10 percent. Testing volumes have probably dropped in half over the past couple of months.

We're working with the Ohio Department of Health on the variants. We do have sequencing equipment. We're doing about 100 a week. We have criteria for those specimen selections: recurrent or persistent infections, a positive test post-vaccine, samples from children, *S* gene target failure, and patients receiving monoclonal antibody therapy. We're building numbers in those categories. Random ones are thrown in there too. I've suggested that we might sequence an occasional negative patient as a good control practice.

My own question for the group is twofold. Is there any evidence that variant testing is affecting patient management decisions? Related to that is: How are you handling requests from clinicians for sequencing information? It's more than just a regulatory question. We don't know what these mean yet in terms of individual patient decisions. And these tests are being done as research. If our labs are reporting them, whether it's a formal report or otherwise, is that a concern for anyone? So my question is about clinical significance and use in patient care and how you're handling requests from clinicians for these results.


Dr. Dysert

*Dr. Dysert (Baylor):* Great question. The only time we initiate an investigation of a variant is by direct request from infectious disease or infection control people, and it's usually around a clinical failure in therapy. I know of no application on the front end where we could turn something around fast enough to affect the administration of monoclonal antibodies, because the studies are incomplete about whether to use monoclonal antibodies in people with a U.K. variant, as an example. So we're kind of straddling the fence, but we've restricted those requests through a pipeline involving infection control and ID doctors only.

*Dr. Henricks (Cleveland Clinic):* We are getting them only from ID as well. Are the results on an individual patient reported back to that ID physician? Again, because it's investigational and surveillance rather than patient validated testing of known significance.

*Dr. Dysert (Baylor):* Right now we're waiting on the state, so we're off the hook because we haven't gotten back in a timely fashion.

**Sterling Bennett, would you like to comment on this?**
*Dr. Bennett (Intermountain):* It's a great question, and we're more in Pete Dysert's situation at Baylor where we can't get results back timely enough to have an impact on clinical decision-making. But based on the kind of questions we get, I'm concerned about the physicians who believe they already know what to do with the results, and they'd love to have them so they can take those actions despite the fact there's no evidence base yet.

**Is this the subject of some of your long conference calls and meetings that are endless in the COVID era?**
*Dr. Bennett (Intermountain):* Yes, it has been a topic of lengthy conversations and it is ongoing, although the longer we talk, the more concerned I get.

**John Waugh, do you have anything to add?**
*John Waugh (Henry Ford):* We're getting questions about the ability to test variants locally, and we're starting that

process now because we have sent samples to the state and they do some sequencing in-house, but they're far oversubscribed and so they're jobbing it out to the CDC and to publicly traded laboratories. They will not give back to us the information on the samples we send to them because they're concerned about contact tracing and patient privacy. We'd like to at least get aggregate information on what variants are circulating among the samples we've referred to them.

**Dr. Dolan is pointing toward, at last, the antibody testing ship that seems to be coming into port, at least in Tulsa. How is it in Detroit?**
*John Waugh (Henry Ford):* There's antibody testing going on, but a lot of it has been under the radar or low profile. I am hearing about people who have had testing done after their vaccinations and some questions about, "Should we be doing this with others?" And then "What to do with the data?"

**Janet Durham, what can you tell us about antibody testing at ACL?**
*Dr. Durham (ACL):* We haven't had an increase in our antibody test needs. We tried to make sure we were educating people that the antibody test wasn't something we would want to test for following vaccination as we are testing for the nucleocapsid.

***Greg Sossaman, do you have a word or two on antibody testing?***
*Dr. Sossaman (Ochsner):* We're bringing up now the new Abbott antibody test for the S protein. We were using the previous assay, which was again the N protein, and it's been interesting to look at the validation to see people we've tested. We had saved samples from those who were unvaccinated versus those naturally infected to see what their antibody levels were versus those who are vaccinated.

It's not calibrated yet so it's not a real unit, but we're seeing people who have natural immunity around the 600- to 800-unit range, whereas people who have been vaccinated are 9,000 to 30,000 units. The immunity of people who have had prior infection is vastly inferior to the immunity of those vaccinated. We have a large transplant population and there's an interest in monitoring those patients, so I suspect we'll begin to do much more of this. We'll definitely begin to see more interest in antibody testing in the next couple of months. 