The laboratory tests of pandemic summer

Karen Titus

August 2020—In March, the COVID-19 pandemic came in like a lion—and has yet to leave, like a lamb or anything else. Instead, it roared through April and May in early hot spots like New York City and New Orleans. As lockdowns took hold, the cautious hope was that by summer the virus would be tamed (if not simply go away "like a miracle" or "as the heat comes in," per several infamous predictions), giving health care providers a chance to exhale before a likely second wave in the fall.

Instead, June and July saw other cities and states hit hard in turn, while many places that appeared to have flattened the curve were starting to see concerning upticks in cases. And rather than planning for a return of the virus later in the year, laboratories are now talking about SARS-CoV-2 as an ongoing presence.

For months the national narrative has called for the country to test its way out of the crisis. "It doesn't appear to be working," says Frederick Nolte, PhD, D(ABMM), professor of pathology and laboratory medicine, vice chair of laboratory medicine, and director of clinical laboratories, Medical University of South Carolina, Charleston. "We can't get ahead."

"It just keeps getting surprisingly worse," says Susan Fuhrman, MD, president, CORPath, Department of Pathology and Laboratories, OhioHealth Riverside Methodist Hospital, Columbus.

As summer totters on, several laboratory experts paused to speak with CAP TODAY about their current work and their expectations for the months ahead. As it turns out, weathering the pandemic feels like one long March.

As Gregory Sossaman, MD, reviews how Ochsner Health has responded to COVID-19 in Louisiana, he calls it "engaging in an iterative conversation. The same things we were focusing on before we're still focusing on now: testing capacities, supply chain, staff. That's what I'm working on day to day," says Dr. Sossaman, system chairman, pathology and laboratory medicine, as well as service line leader, pathology and laboratory medicine.

Dr. Frederick Nolte at MUSC with Julie Hirschhorn, PhD, associate director of the molecular pathology laboratory (left) and April Kegl, technical coordinator of the molecular pathology lab. "We're not on a good glide path right now," Dr. Nolte said of South Carolina in late June.

(Photo: Sarah Pack/MUSC)

Dr. Fuhrman's experience has been similar. It's not as if she and her laboratory colleagues are done cleaning up the mess that was spring. "I don't object to using that word," she says. "It's ongoing."

Not everything is the same, of course. Many of the instruments that laboratories worked hard to acquire are up and running, and the multiple, daily COVID-19 meetings have been dialed back, in many cases to just a few a week. C-suite administrators are no longer wondering what the laboratory does or asking for tours.

But testing remains parlous. Dr. Nolte is still using the word "pivot" with distressing regularity. "It's always been a part of my vocabulary, but never in this way. On a regular basis you're asked to switch to a different sample type, to a different test, to a different testing criteria. It's maddening."

As the virus lingers, so do the questions. The one Dr. Nolte says he's asked most often is astoundingly basic: *What is the diagnostic sensitivity and specificity of the SARS coronavirus PCR test that you offer, Dr. Nolte?*

"My answer is, 'I don't know,'" he says.

He can report the analytical sensitivity and specificity "in excruciating detail," he says. "I can tell you what looks like a strong positive reaction and a weak positive reaction. I can tell you how we performed in proficiency testing programs. I can tell you to some extent how well we compare with other platforms." But months into the pandemic, "I honestly cannot tell you what the diagnostic sensitivity and specificity of this test is."

He unspools more questions in need of answers. "What are the true clinical performance criteria of the test we are offering and will probably continue to offer for some time? The true diagnostic sensitivity and specificity of serology? Are there better markers of disease? Do we need qualitative tests? Do we need to be looking at host response? Do we need to be looking at subgenomic messenger RNA in clinical specimens to figure out, of all these RNA specimens, which ones are actually infectious?"

"This is our stock in trade," he says. "It's not rocket science, but it's the basic stuff that none of us have been able to do."

Laboratories also lack a standard reference material. The search for transport media and swabs, not to mention reagents, continues. Beyond that lie other issues, including capacity—how to build it, how to staff for it, how to share it.

Moreover, deciding who to test, where, and why is a pendulum kept in motion by hospital administrators and government leaders.

Testing criteria have continued to change. Early on, testing was restricted to those with a connection to travel to China or who'd had contact with a confirmed case. When that overwhelmed the public health system, the testing criteria was ratcheted down to include only the sickest patients.

"Now it's wide open," Dr. Nolte says. The CDC's testing priority criteria "basically says, 'Anybody you want to.' Anybody you decide, as an institution, needs to be tested."

While acknowledging the concerns about asymptomatic carriers possibly spreading the disease, he says, "That's a difficult question to answer, because what we've got is a disease that has a nonspecific presentation. If you look at that data, people who were called asymptomatic really weren't asymptomatic at all."

‘We’ve got to have some people with the bandwidth to take a breath and start reviewing charts and determining who really has COVID.’ — Susan Fuhrman, MD

Dr. Fuhrman agrees: “It’s been a huge challenge, testing thousands and thousands of asymptomatic patients.”

With a nod to Michael T. Osterholm, PhD, MPH, director of the Center for Infectious Disease Research and Policy, University of Minnesota, Dr. Nolte calls for smart testing. (Dr. Osterholm and colleagues discuss this approach in their “COVID-19: The CIDRAP Viewpoint” report from May 20.) More targeted deployment, Dr. Nolte says, would have helped labs get ahead of the testing avalanche. Dr. Osterholm’s paper, he says, makes a strong case for not testing asymptomatic individuals, and Dr. Nolte circulated the paper within his institution and suggested it be required reading for hospital administrators and others who make decisions about testing criteria.

Nevertheless, MUSC has begun screening all inpatients. How did they arrive at that strategy? The idea had been percolating for some time, Dr. Nolte says, though the lab had initially pushed back. Two events “tipped us over the edge,” he continues: Several symptomatic patients were apparently admitted to the hospital without being tested, and there was a handful of likely nosocomially acquired COVID-19 cases. Senior leadership then acted.

MUSC is second to LabCorp in providing testing for the state, Dr. Nolte says, and the state legislature gave the university a grant to set up mobile testing sites for screening at-risk patients throughout the state and to have samples sent to the MUSC lab. To handle the “incredible volume,” MUSC has partnered with commercial reference laboratories. Obtaining sufficient swabs and transport media remains challenging, and the best specimen type—saliva, nasopharyngeal, nasal—is anyone’s guess and will likely vary for symptomatic versus asymptomatic individuals.

Using the diagnostic tests for screening “is not how they were approved,” says Dr. Sossaman. “But that’s the need, and that’s how everybody’s using them right now. We’re definitely using it that way.”

There could be good clinical reasons for that, since COVID-19 positivity is associated with higher morbidity and mortality in patients undergoing procedures. And even with serious infection control protocols in place, it seems reasonable to limit the exposure of medical personnel. But the corresponding lack of data on asymptomatic patients is almost crippling, Dr. Fuhrman says. “We have no idea how the tests perform in those patients. We have no idea whether a positive patient is infectious. We have no idea if a negative patient is infectious. We’re in the dark—that’s my biggest challenge.”

Even the analytic sensitivity of the tests—the one thing labs can talk about with reasonable confidence—might be suspect. “We know the analytical sensitivity as far as the minimum viral genomic RNA that the specific probes for each assay can detect. This minimally detected RNA is then mathematically converted to a minimum number of

detected viral particles," Dr. Fuhrman says. "We don't know if we are detecting viable virus or just random fragments of viral RNA."

The emergency use authorization process allowed vendors to obtain their sensitivity figures using contrived specimens from viral particles, she says, including from RNA produced in the lab "that happens to contain the sequences. That's not very clinical, if you think about it."

The all-comers approach has become inflated by demands for testing to help guide businesses, sports, and schools as they shuffle between reopening and shutting down.

Dr. Fuhrman, whose hospital has performed some 12 percent of the COVID testing in Ohio, has been racing to build capacity to handle testing for other institutions, meet requests from companies riding the reopening merry-go-round, and keep ahead of whatever happens this fall. "I've got all three going on," she says. Major sports teams in town, along with other big businesses, are hitting her up for testing, and the governor has assigned hospitals to test symptomatic nursing home residents and asked her hospital to take on more community outreach testing. Her lab is also testing symptomatic prison employees. And when flu season hits, "we're going to have to do way more testing than we're doing now, even if there isn't a resurgence in COVID."

"We've already started thinking about fall," Dr. Nolte says. "Layer a bad influenza on top of COVID—which is not going away, or will ramp up in the fall—and we're going to have a real mess on our hands."

He and his colleagues are considering the use of combination tests that will detect and distinguish COVID-19 from flu A and B in a single test. "Adding SARS-CoV-2 to the routine respiratory panels that are available is going to be the new normal," he predicts.

Waiting until fall might be a luxury, Dr. Sossaman says. "It's not going to be all that long before we see things getting worse."

If things weren't already complicated, "Now we're throwing serology into the mix," says Dr. Nolte. Not surprisingly, serology is also unencumbered by answers.

MUSC had tested more than 6,000 individuals as June was drawing to a close, with a positivity rate of about two percent. "We don't know what to make of that yet," he says.

The laboratory uses the Abbott assay to test for antibodies against the nucleocapsid protein. Positive samples are reflexively tested using an LDT spike protein assay. Concordant results are called positive. When results of the N-protein antibody screening test are negative, the results go out as negative. And a disagreement between the two tests is called discordant. "We think our orthogonal testing algorithm developed by Dr. Nikolina Babic [director of clinical chemistry and POC testing] is a useful tool that can identify potentially false-positive SARS-CoV-2 IgG serology results, particularly in populations with low disease prevalence."

So far, so good. But as Dr. Nolte reviews the data, he's left holding the existential bag: What does it mean?

The spike proteins rise later than the N proteins; if clinically indicated, the lab suggests recollecting the specimen if results are discordant. The patient population for this testing includes health care workers who want to know their antibody status, communities ("Mayors are calling us," Dr. Nolte says), and businesses ("They want all their employees tested"). These selected populations may or may not be representative of the state at large. "That's what we're struggling with—how to understand that."

Physicians are also struggling to answer another frequent question: what to make of a negative SARS-CoV-2 RNA test in the midst of a series of positive results on a patient who's been hospitalized for weeks. What should be done with such information, when physicians are looking to use RNA testing as an indication of cure?

It might simply be a preanalytical problem, Dr. Nolte says. "We're testing at volumes we've never tested before, and it's a little scary when you're generating a thousand results a day." Glancing at his colleagues in clinical

chemistry labs, he says, “For them that’s a piece of cake. But they’ve been doing it for years. Generating results at this scale is new for most academic molecular labs.”

Dr. Nolte also has to figure out discordant results from outside labs. “I can’t tell you how many times I’ve been dragged into, *We have a patient who tested positive at another lab who was sent here and tested negative. What’s wrong with your test?”* The answer, of course, might be “Nothing.” Not every referral lab has earned his confidence, particularly those that have sprung up seemingly overnight.

Even as Dr. Nolte was building up testing capacity, another problem was weighing on him—what he calls the staffing supply chain shortage. “I have the instrument capacity that exceeds the technical capacity to run those instruments like they should be run, 24/7,” he says.

It’s not from a lack of support from hospital administration. “If we put ‘COVID’ on anything, it gets approved,” says Dr. Nolte. While there have been staffing ups and downs over the years in the lab, they pale in comparison to what’s happening now. “I’ve never run into a problem like this in the 35 years I’ve been doing this.”

He mentioned his plight in an Association for Molecular Pathology COVID-19 virtual town hall in June. “After that I got a lot of emails from temporary staffing agencies: *Dr. Nolte, we understand you can’t staff your lab. We’d love to help,*” he says, laughing. He’s tried leveraging capacity from the research community, though that’s not a sustainable solution, he says, because those employees eventually will be returning to their own labs.

He currently has 12 staff who perform COVID-19 testing exclusively. But as other lab employees return from furloughs, “They want to go back to their day jobs,” Dr. Nolte says, which is where they’re needed. COVID-19 volumes are increasing, just as the need for other testing is returning to normal. Moreover, the molecular lab has a larger function as well. “It’s been a struggle to preserve our testing menu,” he says, “because many of those tests are run on the same instruments that are working 21/7”—with that 24/7 goal in mind—“generating COVID results. So now we have to figure out how to squeeze in our routine tests.”

He does have a nuclear option, he says. “We could send out our routine tests to make room for more COVID testing.” He pauses to let that paradigm shift sink in. “To think that we would do that. . . .You’d think we’d take the reverse approach. But everything is so different.” It is, he says, like walking on Mars.

Dr. Fuhrman hasn’t had to resort to layoffs or furloughs, but as her institution prepares to return to more normal routines, she says she, too, will need to figure out how to staff for the already large and ever-increasing volume of COVID-19 testing.

She also counts herself among the fortunate few who haven’t had to struggle with supply chain issues as far as swabs and transport media. “We never had a shortage, which was a big win for us,” she says, crediting the hard work of her “phenomenal” supply management team as well as the vice president of labs, who oversees supply chain.

An unexpected gift came from a large academic research institution, which has been producing batch volumes of viral transport media (“It’s a complicated recipe, so you might as well make a lot of it,” she says) and, as a public service, distributing it free of charge to labs, including hers. “We do the aliquoting into individual specimen collection tubes in our pharmacy under their biological sterile conditions, and make up our own collection kits in-house. It was wonderful to be given this viral transport media, which has been impossible to get. So we’ve got plenty of collection kits. That was one thing we did really well, and we did it early, so we didn’t have that problem.

“Kudos to everyone for making that happen,” she continues. “It’s completely unprecedented. It’s a huge deal. Everybody’s working together and helping one another all across the country.”

Dr. Nolte was watching his state start to wrestle with testing in a way it hadn’t early on. “We were doing pretty well,” he says. When large-scale testing began in the state, primarily anchored in Charleston, the focus was on symptomatic individuals, who moved through the process via telehealth visits and appointments at mobile collection sites. The positivity rate early on was about six percent and steadily dropped, Dr. Nolte recalls. “Until we

reopened.” Positivity rates were in the double digits in parts of the state, and had surpassed the initial rate in Charleston. Weeks later, in mid-July, infections and hospitalizations were still rising.

“Things aren’t really going the way we want them to go in South Carolina,” says Dr. Nolte, “so we’re all a little worried.” He notes that the state was one of the last to shut down as the pandemic began and one of the first to reopen. “We’re not on a good glide path right now.”

In Louisiana, Dr. Sossaman was also watching numbers rise. Unlike South Carolina, however, the graphs depicting numbers of cases looked more like a set of camel’s humps than a trip up a single mountain. When the pandemic first landed, New Orleans was hit especially hard. “That’s when my life as a system chair stopped,” Dr. Sossaman says, and he, along with several colleagues, switched to full-time COVID testing strategies. “It was nothing else for a couple of months.”

They quickly scaled up, bringing on PCR testing, followed by rapid testing. Months later, the scenery still looks the same.

“We’re using every single test every day,” Dr. Sossaman says. “I don’t think we can build out capacity fast enough. We’re still seeing the need for additional capacity throughout the state. We had to build out a whole new lab because we ran out of space.”

How fast are things moving? Says Dr. Sossaman: “We’re still constructing the lab while they’re putting the instrument together.”

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Dr. Fuhrman’s biggest challenge, still, is obtaining reagents, a situation that “has gone off the rails.”

The lab runs five different testing platforms. “That’s the only way I can get enough tests to do what I need to do,” she says. Capacity in June was 1,400 to 1,500 tests per day, but she hopes to boost that to 2,500 as fall approaches.

The normal limitations are no longer in play. “If I want money, if I want space, the system will give me whatever I need,” she says. “If it has to do with COVID testing, it will be approved at the highest level as soon as I present a cogent plan.” The importance of COVID-19 is one obvious reason for this loosening of purse strings, but she cites another factor as well. Throughout the pandemic, “The lab has garnered unbelievable respect from the health system. And we haven’t steered anybody wrong, so they trust us.”

Trust can’t unsnarl supply chains, however. “I just can’t get what I need for love or money,” she says. Vendors can’t deliver, nor do they want to overpromise, she says. That has put laboratorians in another new situation:

Purchasing instruments now entails negotiating for reagents. “That is *never* how it worked before,” she says. “Usually they try to push more reagents than you need.”

Also “completely fascinating,” she continues, has been the vendors’ control of utilization. She has to keep one vendor apprised of how many tests and plates the lab runs, for example, “because they want us to run only full plates. So I’ve got to wait until I have 96 specimens before I run it.”

Vendors track this daily, she says. “They know how many plates they gave us and how many plates we ran, and if we ‘wasted’ any, meaning we didn’t get a test result because we put a plate in partially empty.”

“You can see that this would be a turnaround time problem,” she notes. The onus is on Dr. Fuhrman to manage TAT expectations, particularly for pre-op cases. “If I get a specimen in the lab late Wednesday and have a partial plate, I still have to figure out how to get it tested that night.” Fortunately, she has four other platforms among which to juggle specimens.

But it’s a differential equations nightmare, she says. It’s constant. “And it just gets harder because the volume keeps going up.” Although there has been some sense—in Ohio, at least, at the start of the summer, that “we’re past the bad part”—that is, spring—“from a testing standpoint we’re in the midst of a challenge, the likes of which we’ve never seen before.”

The inability to obtain reagents has also weighed heavily on Thomas Williams, MD, a pathologist formerly with Nebraska Methodist Hospital, who subsequently served as chief medical officer and director of the Division of Public Health for the Nebraska Department of Health and Human Services. Recently retired, he unretired when the COVID-19 crisis hit this spring. “Just helping out,” as he puts it, as a pathologist familiar with public health.

When he began helping support the state’s response to the emerging pandemic, Dr. Williams surveyed laboratories to get a sense of who would be able to perform tests. The answer seemed promising: There were numerous instruments across the state, not only along Interstate 80, but in smaller communities.

That bit of good news was tempered by another response: “No one—*no one*—had any reagents,” Dr. Williams recalls. For weeks, the only COVID-19 testing capacity was in Omaha.

More recently, more devices and reagents are being brought into the state by the federal government, he says. But at institutions that already had an analyzer in place, reagents have remained scarce. One vendor told Dr. Williams that a site he was inquiring about “will get reagents in ‘a few months,’” Dr. Williams says. “The reagent supply in the field has been very, very spotty.”

One of the more pressing problems of the pandemic is that its overwhelming nature has meant no one has had time to think. “We’ve all been reacting,” Dr. Nolte observes. That includes trying to stay on top of the unending stream of information that appears in all its forms, including medRxiv. “That website is really complicating my life,” Dr. Nolte jokes.

No study, it seems, is too small to inspire well-intentioned hope. “Someone gets ahold of it—it could be a researcher, it could be a hospital administrator—the next thing I know, I’m responding to it,” says Dr. Nolte. Hence the stream of studies filling his inbox that involve four patients and somehow conclude that saliva is better than an NP swab.

“What am I supposed to do with that?” Dr. Nolte asks. Even the high-quality, peer-reviewed journals are pushing out information with head-spinning speed. He serves on the editorial board of several journals, “and I know the pressure they’re under to turn things around quickly. The journals are racing to publish data that they think will be interesting and of value. But there’s a fine line you walk between putting information out that you might not be so comfortable with in normal circumstances, and balancing that against the need to know.

“I don’t have a good answer for that, either,” he says.

Equally frustrating, Dr. Nolte says, is that he has researchers "clamoring to gain access to specimens. I know that's part of my job; I know it needs to be done. But it can't be done now."

"There's so much data that's flowing by," he adds, "and so many opportunities to do things that would be of interest and value are just slipping away." (Despite the crunch, he and colleagues with the infectious disease subdivision leadership of the AMP wrote a perspective piece for the *Journal of Molecular Diagnostics* [Nolte F, et al. doi:10.1016/j.jmoldx.2020.06.003] about responding to SARS-CoV-2 and future pandemics.)

Dr. Fuhrman comes up equally empty-handed as she digs for answers. By early June, her institution had tested some 13,000 asymptomatic patients, with a positivity rate of 0.22 percent. "Is that the right use of our test?" she asks. "I don't have an answer to that. I don't know anything about those patients—I just have the statistics. And nobody has the manpower right now to be cranking out clinical studies on this.

"We've got to have some people with the bandwidth to take a breath and start reviewing charts and determining who really has COVID," she continues, echoing Dr. Nolte's earlier concerns about supposedly asymptomatic patients. That will include reviewing chest x-rays and patients' clinical course, then identifying a method to determine who's positive independent of the test result. The gold standard is either another test known to be 100 percent, she says, or a clinical scenario. "And we don't have either." She points to a June 5 *New England Journal of Medicine* "Perspective" piece (Woloshin S, et al. doi:10.1056/NEJMp2015897) that explores the topic in depth—and includes data out of China that indicates an assay clinical sensitivity of 70 percent. "That's appalling," she says. "I'm hoping ours is better than that. But we don't have any idea."

Another key study—when there's time—would be one looking at recuperative antibodies. "That absolutely needs to happen," she says. Did patients who tested negative produce antibodies? "I would love to know that." And how long do very sick patients shed the virus? "We don't know that either."

She doesn't anticipate a need for additional prognostic tests down the road, but the fact that COVID-19 patients are hypercoagulable seems like a crucial clue. "We need to know who we should be following and when we should act. When do we look for coagulopathy?" As protocols emerge, she anticipates relying on straightforward lab tests such as D-dimer and C-reactive protein; there will likely be a role for markers of cytokines as well as coagulopathy, she predicts.

She's keeping an eye on innovative work being done by clinicians who've seen vast numbers of COVID-19 patients, including those in New York City. "But it hasn't hit the press," she says, "because who has time to write about this stuff when you're taking care of patients?" She and her colleagues did evaluate the clinical performance of three molecular assays in symptomatic patients during the initial height of the pandemic (Cradic K, et al. *Am J Clin Pathol.* 2020;154[2]:201–207), "but putting it together was a real struggle."

Absent a robust literature, Dr. Fuhrman has turned to (among other sources) a podcast, "This Week in Virology," which drops twice a week and is hosted by PhD virologists. Particularly interesting, she says, are the conversations with contributor Daniel Griffin, MD, PhD, of Columbia University Medical Center. "He's got some great information about what they're seeing clinically," she says, adding that she and an ID colleague listen and discuss content regularly. "It's phenomenal," she says. "We're just eating it up."

Dr. Fuhrman also oversees antibody testing ("I'm all things COVID," she jokes) and is working with medical staff to figure out how to use it to add value. The test is not useful for diagnosis, obviously, but it might augment information on confusing and complicated cases.

The larger use for antibody testing remains in the public health setting, of course, but it's still a foggy area for the public. "And the clinical use is even confusing to physicians," Dr. Fuhrman says. Indeed, she had just worked with the medical director of her clinical chemistry lab to write an educational piece on serology for their physicians. "Again," she says matter-of-factly.

Dr. Sossaman also reports a sense of déjà vu in his conversations with clinicians. He's frequently asked about

discrepancies between test results, or between results and clinical sensitivities. Or, colleagues might ask about using antibody testing preoperatively. “We continually seem to answer the same questions for people,” he says, with no trace of impatience. “There’s so much information coming at people.” That’s turned the lab into a de facto town crier.

When one vendor told him they were starting to see reports of higher positivity rates in some areas, for instance, it was a possible indication that the curve wasn’t as flat as some had presumed it to be. “So I’ll pass that message along to my clinical colleagues and let them know what’s going on.” Which, of course, will spur more questions. “But that’s our role,” Dr. Sossaman says. “We’re sort of a central clearinghouse for information.”

That’s especially valuable, he says, when information is confusing. “We tell our colleagues, *This is what we know—let’s decide together what to do about it.* We’re very upfront about what we know, what we don’t know, and what we’ve seen in the literature.”

In some ways, the lack of information has been freeing, Dr. Sossaman says. “We’ve made a little bit of a transition in our way of thinking. Rather than being the deliberate voice, which the lab always is, we’re the proactive voice.”

That’s due in large part to that Grand Canyon-sized lack of data. Much as he’d like to talk about the test performance in the usual terms, he simply can’t. Hence his pivot. Instead of responding *Yes, but* . . . , Dr. Sossaman and his lab colleagues are pulling a page from improv and learning to respond, *Yes, and*. . . .

Is a colleague asking about saliva testing? *Sure, let’s look at it.* Swab and saline? *Let’s go ahead and look at it.* Do more testing? *Let’s see what we can do.* “Whatever is put in front of us,” Dr. Sossaman says.

The natural inclination in the lab, driven as it is by process and procedures and heavy regulation, is to safely pump the breaks, so to speak: *Where’s the data? What’s the need? Can we do that? Do we have the staffing? How much is it going to cost?*

Good questions, all—but not at all productive in a pandemic, he says. “That kind of thinking would have gotten in our way. So we quickly changed our stance to, *How can we make it happen? And how can it be as fast as possible?*”

The pandemic hasn’t changed everything, of course. “We’re still scientists,” Dr. Sossaman says. “We’re still realistic.” But waiting for the perfect test, at least for now, is off the table. Instead, they’re bringing a new shade of meaning to reflex testing. “Our answer is reflexively, *Yes*. And then we figure out a way to make it happen.”

One thing that hasn’t happened, much to the dismay of many in the lab, is a more coherent and cogent federal response to testing.

Those who’ve spoken to CAP TODAY, on the record and off, are quick and careful to say they’re not talking about politics. But concerns about politicization weigh heavily over testing, they say, as does the fact that individual states are charged with figuring out how to manage testing, sometimes in competition with one another. Policy and government have become almost unspoken pre- and postanalytical variables, though they have nothing to do with testing itself.

“And yet it’s all a lab problem,” Dr. Nolte says.

Eyeing the “intersection of public health, politics, panic, regulation, fear of the unknown, and media hype,” Dr. Nolte sees a pileup. “This became a political event rather than a public health event. That’s where this really went bad,” he says.

The lack of a national health system in the United States has added to testing woes, Dr. Fuhrman says. The dispersion of individual hospitals and health systems spread across 50 states was a liability against a virus that doesn’t respect man-made borders. And any wider response “has been appallingly disorganized,” she says.

That includes reporting, which Dr. Fuhrman calls a nightmare. Labs had to submit reports to three different

agencies—state, county, and federal—all of which use different forms and require different information. “That’s inexcusable.”

She called on groups such as the CAP, CLSI, and AMP to lobby for changes to “stop the madness,” as she puts it. “You want us to do the tests, we can do it. But the amount of time we’re spending just writing software because they cannot get their act together—that’s just not right.”

Her comments came weeks before HHS issued, on July 10, new requirements for reporting COVID-19, including for laboratories (https://j.mp/HHS-reportingfaq). Responding to that change, she voiced a concern that many shared—that the new requirements bypassed the Centers for Disease Control and Prevention.

“To use precious lab resources appropriately, we should have a streamlined reporting mechanism to a single entity, presumably the state, as they have generalized authority and jurisdiction over public health,” she wrote in an email. “The federal government should obtain the data from the states. We shouldn’t be cutting the states and CDC out of the data flow nor should we have to provide two, three, or four data reports.”

The change involves a technical challenge as well, she wrote. “Many of the new required elements of reporting require information from patients that we do not normally gather nor do we have discrete data fields in our IT systems to record the data.”

The aforementioned pressures on labs to justify their use of, and requests for, supplies and reagents may point to another issue, says Dr. Sossaman, whose vendors ask him for a strict accounting of how he uses resources. “They say, *We can’t just send you this. Are you really running these tests?*” He suspects it reflects the tremendous pressure vendors are under to justify their own actions.

“It’s been very confusing from a national perspective,” he adds. He hears conflicting messages from vendors about how the federal government is maneuvering reagents and supplies “to affected areas or snapping them up and redirecting them.” It’s a tricky situation, he says, because there’s no transparency around the process. The only thing that is clear, he says, “is that there’s absolutely no national testing strategy. It really shows.

“We need one,” Dr. Sossaman continues, in no uncertain terms. Leaving the states to fend for themselves isn’t working, in his view. Encouraging competition between local and regional entities has led to imbalances in the supply chain, and it’s been left to vendors to rebalance. Large systems like Ochsner have an advantage, he notes, and disparities in health care delivery will only increase.

Dr. Fuhrman concurs that vendors are following the directives of the government, and that the process remains shrouded in mystery. “I don’t know their secret sauce,” she says, adding that she’s been told one vendor has been lobbied by a congressional delegation. “So if you don’t have your governor or senator on the case, forget it,” she jokes. She, like others, notes that there’s been unprecedented cooperation between labs over the course of the pandemic. At the same time, she can’t starve her own system, either. “It’s been really, really hard,” she says.

‘They were very adamant that we were swimming in reagents, and I can

tell you that outside of Omaha, nobody—not one lab—had reagents.' Thomas Williams, MD

A national strategy would make it easier for sites with unused capacity to support labs that are getting slammed, Dr. Sossaman suggests. It would be a huge step to have a national database—"almost like a dashboard"—to monitor unused capacity and allow, say, Texas, to send testing to New York. "How does that *not* make sense?" he asks. "Right now, everything is so fractured." It would be fairly easy to put together such a scheme, he says, but it would require federal authority to pull it all together.

Dr. Nolte pulls no punches when he considers the national scene. Current use of testing resources "isn't the best utilization. We know it's not sustainable."

"I'm sorry, but we have had a total failure in leadership at the federal government level," he adds. "I think that if the current Administration realized this was a significant problem, and that they need to get the best and brightest people working on it, and to step out of the way, things might have gone differently. It's been a mess. Unfortunately, there are lives at stake here. Lots of lives."

He speaks highly of medical leaders such as Deborah Birx, MD, and Anthony Fauci, MD, but they don't represent the clinical lab practice—a frustrating situation that he sees being played out on the local levels as well. "We can't get a seat at the table," Dr. Nolte laments.

The inability to amplify the lab voice has also bothered Dr. Thomas Williams. Nebraska, rarely a state to draw attention to itself, has maintained its unassuming profile during the pandemic as well, managing to stay out of headlines and dealing with numbers that produce neither scary spikes on graphs nor maps colored red. But it, too, has been affected by the lack of a national test strategy, and along with others, Dr. Williams has felt the frustration of having non-lab voices calling the shots. "In the course of surveying the state, I talked to a number of laboratory people and they were *enormously* frustrated, just like the reps were. They couldn't blame the reps. The decisions were made above them."

That's important for two reasons, he says. One is on the technical level, obviously. "The other is the Realityville test of what's out there." As he listened to physicians on the federal level—whom he admires—talk about the ability for labs everywhere to perform COVID-19 testing early on, and the reports of reagents being widely distributed, he knew his colleagues in the state had a different story to tell. "I'm looking at Nebraska, and it's sucking canal water.

"From my perspective, they should listen more to what is really happening out there," Dr. Williams continues. "They were very adamant that we were swimming in reagents, and I can tell you that outside of Omaha, nobody—not one lab—had reagents. And that's a lot of labs. I practically threw something at the TV on a couple of different evenings" when he heard nonphysician leaders proclaiming their success in distributing reagents. "That made me very angry."

For all the changes wrought by COVID-19, some basics in the laboratory have changed not one bit.

Dr. Sossaman has been able to work so proactively with his clinical colleagues because the lab had already had deep bonds with them. "It's been interesting to see how those relationships really crystallized during this period of time," he says.

It's a point Dr. Williams returns to as well. His years of working with public health professionals, other professional associations, and vendors, as well as his time working in government, were invaluable as he helped prepare communities and counties in Nebraska for SARS-CoV-2. "There isn't going to be cavalry coming in to take care of it

for you," he says.

His own survey of test availability turned out to be far more accurate than the map distributed by the federal government. "I knew where every assay analyzer was," Dr. Williams says. "They missed a whole bunch of them. They said, 'We have a map of where all the tests are in your state.'" Dr. Williams's response is swift: "No, you don't. You have a map of where *some* of the tests can be done.

"I don't know where they got their data," he says. But he knows where he got his—by reaching out directly to colleagues, many of whom he already knew.

Dr. Fuhrman sees another steady aspect in the midst of otherwise relentless change. The laboratory has "always knocked it out of the park," she says. But now the stands are filled with people and the game is being broadcast. "We step up to the plate all the time," she says. "I don't know that it's ever been so public. We've always made a huge difference, but it wasn't as noticeable."

The camaraderie and can-do response from her laboratory colleagues has buoyed her. "Everyone has just dug in, and we're working all the time, weekdays, weekends, round the clock, and everyone is doing whatever they can to help patients. It's phenomenal. It's been a defining moment for the laboratory."

Oddly enough, it's one she almost missed. "I was originally planning on retiring in January," she says.

Karen Titus is CAP TODAY contributing editor and co-managing editor.