

In urinalysis, reflex algorithms and other efficiencies

March 2023—*Urinalysis was at the heart of a Feb. 7 discussion between CAP TODAY publisher Bob McGonnagle; Ron Jackups Jr., MD, PhD, of Washington University School of Medicine; and Jason Anderson of Sysmex America. “There’s a lot of room to explore what the optimal parameters are to use with the best specificity and sensitivity for a reflex to the sediment analysis or the culture,” Anderson said. Here’s what he and Dr. Jackups said about reflex testing, automation, and middleware.*

CAP TODAY’s guide to urinalysis instruments begins [here](#).

Since the urinalysis roundtable in December 2021, three things continue to be hot issues regardless of instrumentation, field of analysis, and subspecialty. Number one is automation in workflow, having something that’s robust for high volume, low staffing. Number two is the need for fit of an instrument line. In other words, there’s a core lab urinalysis instrument that’s ideal and yet there are smaller clinics, hospitals, all kinds of sites that can benefit from the same technology but in a differently configured unit. Number three is understanding if we’re extracting the optimum clinical information from the analysis in fields like hematology and urinalysis.



Dr. Jackups

Ron Jackups, talk to us about reflex testing in urinalysis and then more specifically about what you’ve been working on at Barnes-Jewish Hospital.

Ron Jackups Jr., MD, PhD, associate professor of pathology and immunology, Washington University School of Medicine, and associate chief medical information officer for laboratory informatics, BJC HealthCare: Reflex testing in general has two big benefits. The first is it focuses the diagnostic process, which reduces waste. We have seen in urinalysis and other areas that providers, rather than order a test and wait for the result and then order another test based on that result and wait for the next result, et cetera, tend to do what we call shotgun testing—they order all the tests they think might be relevant at once and then react to the results after they get them. This is wasteful in many situations if the tests further down the line were not necessary and can also be dangerous if one of the tests down the line is a false-positive. Part of the goal of reflex testing is to identify situations where there’s a low diagnostic value and high risk of false-positives in future tests that could be prevented by simply not doing them. That’s the first reason to do reflex testing.

The other benefit, which is smaller but simpler and particularly relates to outpatients, is convenience. You do a single draw of a sample and the patient does not have to be redrawn. If it is an outpatient, they don’t have to come back for a future redraw. Reflexes provide the same kind of turnaround time that shotgun testing would give but without the inconvenience and with a much better diagnostic process.

The impetus for making these reflexes at our institution was what we saw as high false-positive rates of urine cultures, and I don’t mean analytically false-positive. We’re actually diagnosing asymptomatic bacteriuria. Patients who really did not have symptoms of a urinary tract infection but were tested anyway by a urine culture were found to have a positive, and then despite that not being a cause of the patient’s problems, were treated with antibiotics.

This is not only a waste of our antibiotics and a potential trigger of antibiotic-resistant organisms but also a potential financial penalty for the hospital because the Centers for Medicare and Medicaid Services penalizes systems that have a high rate of catheter-associated UTIs [CAUTI]. And if you happen to find an asymptomatic

bacteriuria in a patient with a catheter, that counts as a CAUTI and triggers financial penalties as well. That was one of the drivers for making the reflex.

What benefits have you seen?

Dr. Jackups (Wash U): We have seen a dramatic drop, by almost half, in the number of overall urine cultures ordered. The positivity rate on urine cultures has not changed appreciably, which means overall we're seeing a drop in the number of positive urine cultures but not a drop in the return on urine cultures. It means we're doing a better job of selecting the patients who are likely to have UTIs.

An outstanding feature of the field of hematology and urinalysis both is how much effort has been devoted to things like urine culture and urinalysis and the manual differential, which is often at excessive numbers in the field of automated hematology because people haven't properly understood parameters for those analyzers. Sysmex is one of the companies that can work on both sides of this avenue, in urine and hematology.

Jason Anderson, would you agree the parameters aren't always well understood? And can you speak about general customer recognition and acceptance of improvements made in urinalysis that lead to cost savings and better care?

Jason Anderson, MPH, MT(ASCP), senior product manager, urinalysis solutions, IVD product marketing, Sysmex America: Yes, I agree. One of the many benefits of flow cytometry is that we're measuring both chemical and physical properties of particles in urine. Our laboratory customers recognize that the accuracy and precision that come with flow cytometry technology means the technology lends itself to high-quality results, which can offer invaluable information in the clinical care pathway for the patients they serve. When it comes down to enumerating particles and using those to make decisions about patient care, whether you're going to culture or do additional testing, our customers comment positively about and recognize the value of having good-quality, trustworthy results via flow cytometry.



Anderson

Do you have other customers who are as interested in the application of reflex testing in urinalysis as described by Ron?

Jason Anderson (Sysmex): Yes, and I agree with Dr. Jackups' commentary. With staffing challenges and economic pressures ever present, the need for laboratories to optimize resource utilization, improve turnaround times, and reduce costs, whether it be reagent or labor costs, is becoming increasingly critical. Optimized reflex testing can play an important part in improving those things. Our customers are looking to their in vitro diagnostic vendors and their peers for guidance on reflex testing. Unfortunately there's not as much evidence-based research as there needs to be in urinalysis for this type of exercise in terms of what the optimal criteria are or the best practice is for reflex testing. I have spoken with clinical investigators who are interested in looking at the performance of certain urine parameters in different populations, whether it's neonatal, obstetrics, transplant, immunocompromised patients, et cetera. It's highly likely that it's not one-size-fits-all criteria for reflex testing; it depends on the population. There's a lot of room to explore what the optimal parameters are to use with the best specificity and sensitivity for a reflex to the sediment analysis or the culture. Those are important questions that still don't have definitive answers or answers as good as we need to make better reflex testing decisions.

Ron, urinalysis is not a field that's rich in research compared with many other areas of the laboratory. But when we talk about reflex testing, I know many CAP TODAY readers have a certain nervousness about ordering their own test. In other words, "We're determining we're going to generate more test

volume on our own word.” Is that a fairly widespread anxiety?

Dr. Jackups (Wash U): Yes, it is. We do not want to be the people who dictate what tests need to be done on patients. And we need to have some sense of humility because we are not the people in the room seeing the patient, knowing the patient’s problems. Even if we cite clinical research that says otherwise, it’s important to understand clinical research is done on a group of people and the average findings on that group do not necessarily relate to the specific patient in the room at the time. Starting with that humility, it’s important to know that any change we make should not be the sole decision of the laboratory, and these decisions need to be broad policy decisions made with the input of the stakeholders.

When we make these decisions, we have extensive communication with the services that are using the test and with clinical experts who treat patients who have these tests drawn on them. The collaboration we have for urine reflexes is done with an incredible amount of input from and work with the infectious disease experts at our institution, particularly the infection prevention team and the microbiology lab.

Do you go before a certain body to establish that there’s an approved policy in place at Wash U for this sort of reflex testing in urinalysis?

Dr. Jackups (Wash U): We have several governing structures. We created a clinical lab steering committee, which is a group of laboratory leaders that represents the laboratories in the system, and that’s often where these questions get asked. In the course of that discussion we identify the stakeholders outside of the labs who are going to be involved in the discussion. None of these teams by themselves have absolute power to make those decisions. But in coming together and having this consensus and the reputation that we work to improve patient care and reduce waste, we are able to make decisions and get people in the hospital to accept them.

Jason, does this sound familiar to you? Do you have customers trying to do something similar?

Jason Anderson (Sysmex): It does sound familiar and we do. And to Dr. Jackups’ point, no one has absolute decision-making power here. It falls to the laboratory in conjunction with its medical director and clinician staff to decide what’s appropriate for their patient populations when determining and employing reflex testing algorithms in the test menu. One of the things that plagues urinalysis is there are not a lot of clearly defined best practices when it comes to how to report and interpret some urine parameters. What are the best units in which to report a specific urine particle? Is semiquantitative high power field/low power field range reporting for particles ideal or can we better take advantage of improved technology that can return a specific value for particles such as red and white blood cells? There is not a lot of strong, concrete evidence and scientific study yet surrounding questions like these. It opens things up to questions: What are the parameters of choice? Where do the specificity and sensitivity need to lie to make these reflex decisions to meet the greater good of the population and provide the best patient care? Investigators are beginning to think about these aspects more, and we hope to see exciting research in the near future that can give laboratories a jumping-off point to make better decisions on when to reflex.

To Dr. Jackups’ point, the clinician needs to be able to make the best decision for their patient in terms of test orders. Reflex testing can help laboratories with optimizing utilization, which can significantly impact turnaround times. If a laboratory is performing unnecessary testing—testing that would not have been performed if governed by optimal reflex test criteria—then it is spending time and resources that could be used for other, more value-added tasks.

Dr. Jackups (Wash U): There is an additional concern that when you create a reflex, you are reducing the options of the provider to a one-size-fits-all practice. One way to mitigate that, at least in the beginning stages, is instead of having a single reflex, we have three options for the reflex: one that will not end in a culture—we call that the urinalysis reflex from macroscopic to microscopic, to do appropriate urinalysis testing for a patient when UTI is not suspected; one where they do suspect UTI, and that can end in a urine culture if all the right criteria are met; and a third for neutropenic patients, recognizing that neutropenic patients may not have the white cell response that someone without neutropenia may have, and that has a lower threshold to trigger a urine culture.

I agree with Jason that we have not fully worked out in the literature a universally best practice, but we can mitigate it somewhat by giving the providers options.

As an observer, this sounds to me like a wonderful project for a clinical pathology fellow. Have you had anybody volunteering at Wash U?

Dr. Jackups (Wash U): We do a lot of quality improvement in all areas of the laboratory, and we've incorporated that into our residency education. I teach clinical informatics and it involves both the data gathering and the actual changes you make in the system, and this is one example. When we created the reflex, it was so new for us to gather all these governance pathways that we didn't engage our trainees as much as possible. But since then we have really made it robust.

Now we are looking at ways to improve the neutropenic reflex I mentioned, and the idea came to us from a medical student who was rotating with me on a clinical informatics elective. She had noticed that people weren't ordering the neutropenic reflex in neutropenic patients, and it was an opportunity for improvement. So she and I and others in our department have been working on a project to make those improvements. It just took a student noticing on the floor that something wasn't happening. It is driven by an openness to keep reassessing current process, looking for improvements, and engaging everyone. This isn't just to improve patient care but a part of the educational experience.

Jason, I'm sure you have other customers in advanced academic laboratories that are working along some of the same paths.

Jason Anderson (Sysmex): Yes, we do. I have spoken with a few potential investigators who are interested in looking at what the optimal urinalysis criteria are for making better clinical decisions in different populations. Urinalysis is ripe for growth as diagnostic technology in urine screening becomes more advanced. It is feasible that we could see future UA platforms flag for the suspected presence of atypical cells in urine, which could potentially make it possible to effectively screen for bladder cancer and perhaps reduce the need for more invasive procedures. There are still many things we can't do now or don't do as well as we could. There are a lot of different avenues outside of urine culture to improve the diagnostic and/or screening utility of the urine sample.

It would be an enormous desideratum if that could be achieved for detecting bladder cancer. The flow cytometry application in particular is going to suggest this sort of rare cell discovery event. Is that correct?

Jason Anderson (Sysmex): The nice thing about flow cytometry is if you can stain it and measure it, you can probably gate it out at some point. Are we there yet in any type of routine way? Certainly not. But the power and the ability to expand direction in flow cytometry is one of the benefits of that technology. We're always thinking about how we can better discern or detect particles that maybe aren't detected routinely and what the clinical implication and the utility of those types of things are. Again, there's not as much research in these areas as we would like, so hopefully we will see more interest in advancing this body of knowledge.

Jason, with the Sysmex UN-Series are you seeing increasing numbers of laboratories putting the urinalysis instruments on their core line?

Jason Anderson (Sysmex): Yes, especially in the past six months. We've had a lot of customers, big and medium size, ask about connecting urinalysis to total lab automation to create those optimizations and efficiencies that labs are sorely in need of. Sysmex is working toward connecting to TLA. We have some advancement there and we have the first urinalysis system that connects to TLA. We expect that trend to continue as labs work to become more efficient on their urinalysis bench. The big driver is creating efficiency when you have a shortage of skilled technologists.

Ron, does that sound like something you'd like to do in the clinical laboratories at Barnes-Jewish?

Dr. Jackups (Wash U): Yes. We have a large laboratory and most of our routine testing—CBC, chemistries, and now even coags—can start from there, and being able to automate that process would be a huge benefit for macro and micro urinalysis.

Can you comment on the staffing situation you're facing in St. Louis?

Dr. Jackups (Wash U): It remains a problem. A lot of young people aren't looking to be laboratory technologists, and a lot of our experienced lab technologists are getting closer to retirement. The other threat is that as we move into

more complex and patient-centered testing, we want our technologists to focus on that and less on routine testing. To the extent we can cut out the manual steps related to routine testing, that gives us more opportunity to expand into improving the technology that relates to more specific testing for our patient population.

It seems clear that in many fields, particularly in the clinical laboratory, we have routine testing that needs maximum automation, maximum application of reflexes, and then increasingly we have complex testing on patients with interesting and problematic conditions. Is that what you're suggesting, Ron?

Dr. Jackups (Wash U): Yes. The more we can automate routine testing so that it's no longer the driving force of manual work in the laboratory, the greater the number of avenues toward innovation.

Jason, do you see this as well among your customer base?

Jason Anderson (Sysmex): Yes. The Sysmex UN-Series Automated Urinalysis Solution is designed to offer customers a largely hands-off, fully automated, and scalable testing experience on the urinalysis bench. It begins with the analyzer technology and the ability to use flow cytometry to measure particles in an accurate, precise, and standardized way. This leads to the potential ability to automatically autoverify a significant amount of the urinalysis workload without operator intervention. Additional efficiencies can be realized by incorporating TLA connectivity or adding the integrated TH-11 Urine Sample Decapper Unit. We want to help our customers get away from having to perform manual processes in urinalysis that don't add direct value; it's just busywork. We're trying to take care of that for laboratories so they can reallocate their staff to the more complex testing that requires their expertise.

Over the past few years every instrumentation roundtable I lead turns into a discussion also of informatics. Are we getting the results from these instruments not only into the LIS but also into the EHR resulting? Where are you with that in urinalysis testing at Wash U, Ron?

Dr. Jackups (Wash U): Most of the results we report are discrete, and discrete results are always better than text-based data, as far as informatics goes. We have a pretty good ability to pull that. The metadata surrounding the test also matters. That includes turnaround times and identifying contaminated cultures. That data needs to be put into an area where we can pull it easily and pull quality reports that our labs can use.

The lab information systems, to their credit, have done what they can to provide that data, but we often have to think about customized solutions—not just because the lab information systems can't do it but also because every system is different. We have our own quality goals. We've perceived our own problems and we need to build tools to that. The way to facilitate customization is to liberalize the data, make it as easily accessible as possible, and I think we're seeing that. The information systems vendors have put in extra effort to make it easy for organizations to pull the data, put it into data warehouses where we have more direct access and ability to pull giant amounts of data in short periods of time, and then crunch the numbers to do data analysis to answer specific questions, in this case quality questions to improve our practices.

Jason, Sysmex has a well-defined offering in middleware in the hematology space. Can you tell us about middleware in the urinalysis arena?

Jason Anderson (Sysmex): The Sysmex UN-Series has an integrated middleware of sorts. It's the brains of the operation, the Urinalysis Data Manager, or UDM, and it's included with all UN-Series solutions. One of its primary functions is to act as the single interface communication point on the UN-Series. The UDM coordinates and manages all urinalysis test orders and results data between the LIS and the connected urinalysis analyzers. The software makes it simple for customers to create customizable urinalysis rules for cross-check or reflex purposes, or both, based on their standard operating procedures. Additionally, the UDM provides an efficient means for the operator to manage, review, and release patient result data, when necessary, from all integrated analyzers on the urinalysis line on a single screen. Remember, with the Sysmex technology it is possible to auto-release those urine samples that have no abnormal flags or other indications for review.

For laboratories looking for greater levels of overall test workflow optimization, clinical data organization, and comprehensive management reporting, we have our optional, intuitive, and secure cloud-based software, Sysmex

Caresphere Workflow Solution.

As a former laboratory manager, now working as a product manager, I'll put on my laboratory manager hat. Advanced reporting functions of middleware allow laboratory management to generate and look at big data in ways we weren't able to when I was in the laboratory. Looking at things like test utilization and the rate of reflex or number of times a rule was triggered is pretty commonplace and can provide a wealth of decision-making and workflow optimization information. I see the potential to look holistically at more nontraditional uses of this aggregate big data to more efficiently evaluate subpopulations to determine more appropriate reflex criteria. Or perhaps look at the quality of urinalysis samples, being able to view data that shows where you might have poor collections, contamination, or preanalytical conditions that could have been avoided and even identify whether a particular source—outpatient site, floor—has a higher than expected defect rate and take steps to educate and improve sample quality. Advanced middleware is the driving force to being able to gather and look at big data in ways we aren't currently. There are a lot of avenues to take.

Dr. Jackups (Wash U): I want to emphasize the importance of middleware because we have multiple vendors for multiple systems, and that includes the analyzer systems, the lab information systems, and the EHR. Right now we have different vendors at our institution doing those three things differently. It is important to be able to connect all three, and middleware is critical to being able to connect the analyzers to the LIS. But it's also important because the same system is not always the best source of data. We try to get clinical data out of the EHR but sometimes we need to go to the source, and the middleware sometimes is that best source of truth of data that didn't pass all the way into the EHR. For each quality problem we're trying to address, we look at each system individually and say, "Which system is going to give us the best source of data?" Then we compile that into the data warehouse. It's another reason middleware is critical to our functions. □