Urinalysis: Efficiency, utility, and the 'movement in the field'

December 2021—*Four experts met on an Oct. 12 call to talk with CAP TODAY about urinalysis—the newest platforms, what labs need, labor solutions. CAP TODAY publisher Bob McGonnagle asked the questions. Providing their perspectives were Matthew Rhyner, PhD, MBA, Beckman Coulter; Jason Anderson, MPH, MT(ASCP), Sysmex America; Megan Nakashima, MD, Cleveland Clinic; and Keri Donaldson, MD, MSCE, Solvd Health and Penn State. Here's what they had to say.*

CAP TODAY's guide to urinalysis instruments begins here.

Matt Rhyner, tell us about the exciting news we heard from Beckman Coulter at AACC.
Matthew Rhyner, PhD, MBA, VP and general manager, urinalysis, Beckman Coulter: We were excited to launch our DxU Iris integrated workcell featuring new versions of our digital microscopy and chemistry analyzer. It brings together workflow enhancements for our customers from a software and hardware perspective while retaining what they like about the digital microscopy platform, in particular with helping reduce manual reviews and making sediment analysis under a microscope unnecessary. We offer new zooming features and software workflow features, an enhanced aspiration module, and load/unload stations for higher-capacity customers. Installations will start this month.

Jason Anderson, is Sysmex seeing a need to integrate platforms within a network and have scalable platforms?
Jason Anderson, MPH, MT(ASCP), senior product manager, urinalysis solutions, IVD product marketing, Sysmex America: We see continuing demand for scalable and integrated laboratory testing solutions, and urinalysis is no exception. Our customers desire standardized technology from test strips to urine particle counting to ensure the comparability and continuity of results from their large core labs to their smaller stat labs and clinics. Our UN-Series Automated Urinalysis Solution is unique in that it employs scalable analyzer modules, and with this modular design, health networks can build right-size urinalysis solutions to fit their workflow needs. In addition, Sysmex will introduce the Caresphere Workflow Solution for Urinalysis in the near future. With this technology, our customers will be able to further drive efficiencies in urinalysis processes and workflow across their organization through rule standardization, on-demand digital information, and management reporting capabilities.

Megan Nakashima, tell me about your need for and experience with integrated, scalable platforms at Cleveland Clinic, not only in the laboratories you run but in the institutions you serve within the network.
Megan Nakashima, MD, medical director, automated hematology, and staff pathologist, Cleveland Clinic: We see the need for being able to flex workflow wherever we can within a site, and if possible between sites. Like a lot of large systems, we have not only hospitals but also a plethora of small clinical sites that may or may not have the space or expertise to do this type of testing. In addition to being able to network one analyzer between people, having a more harmonized system that is scalable is also nice. If you have a line that uses the same strips—that goes from a basic strip reader to the full UF system—that to me has value.

Keri Donaldson, one of the themes we've always had is whether it's possible to do more with urinalysis in terms of the total clinical care of the patient. Do you have a feeling about that?
Keri Donaldson, MD, MSCE, CEO, Solvd Health, and director of clinical genomics, Institute for Personalized Medicine, Penn State College of Medicine and Milton S. Hershey Medical Center: A significant amount of data is generated on somewhat of a ubiquitous fluid sampled commonly within the hospital system. And Beckman Coulter and Sysmex have moved the automation significantly as well as the reproducibility and the large amount of information that's generated from these cells, sample to sample. It allows for the ability to ask additional questions or get clinically meaningful results from the same sample.

We have done historic early data work on using the images, whether they are images generated on a specific

bacteria that could be isolated or overall the data generated from flow cytometric analysis, to talk about the types of bacteria present or not present. We did early work with Sysmex Japan talking about the type of bacteria that's present and starting to move toward resistance profiles. None of that work is clinical in the U.S. yet. But once you talk about high-throughput, highly reproducible data points in the urine, there is more clinical information in the samples.

Dr. Rhyner

Matt, can you speak about the scalability of Beckman Coulter urinalysis solutions across larger networks and geographies?
Dr. Rhyner (Beckman Coulter): We offer that through our clinical informatic solutions. Specifically, our middleware solution allows for harmonization of processes across sites and within hospitals. We have a Command Central feature that allows multiple workcells to be operated from a single point within a single hospital. We have a variety of solutions that harness advanced software tools to help with scalability, flexibility, and standardization. Our partnership in the U.S. with Arkray offers semiautomated and fully automated urine chemistry strips that are fully harmonized. So we offer a variety of solutions from small satellite hospitals to larger core labs, higher-volume facilities.

Megan, following the discussion from Keri, is it your view that urinalysis through the better analysis of what we've identified will prove to offer more clinical value?
Dr. Nakashima (Cleveland Clinic): There are a lot of possibilities. Flow cytometry in general is such a powerful tool that I have a feeling we're not leveraging it enough in many different fields, particularly this one. At the same time, we're seeing work being done with image analysis. If you were to go straight to an imaging-type system, there could be room there to get more data from what you're looking at.

A standard desire or demand in urinalysis has always been to lower the percentage of manual reads. Megan, what's your current manual review rate at Cleveland Clinic?
Dr. Nakashima (Cleveland Clinic): I believe that number is three percent—very low.

Jason, is three percent a possible outcome for anyone, not just specialists, using your instrumentation and software?
Jason Anderson (Sysmex): Correct. With our UN-Series solution, the brunt of the traditionally manual urine microscopic work is done automatically via fluorescent flow cytometry technology. Think of it as being similar to an automated differential in hematology—we're doing that with urinalysis. We're able to, in a standard, precise, and accurate way, measure and enumerate those particles. And for any particles that need to be subclassified, like crystals and pathologic casts, we have optional microscope-quality digital imaging to automate urine particle location for efficient confirmation when needed. We eliminate the need for manual microscopy with those two methodologies.

Matt, same question: Can you approach this rate of three or four percent?
Dr. Rhyner (Beckman Coulter): Yes, we have several case studies with those exact figures.

There are opportunities to improve the on-screen reviews and the amount of user interaction. We're talking about driving down the number of touches required to produce reliable clinical results, at least in the standard urinalysis domain.

What Dr. Donaldson brought up about the additional information that could be derived from urine is interesting.

Right now we report quite a few subcategories of particles, not all of which doctors use clinically; they use a much smaller subset. But medical technologists like all that information, so it's a question of what's most useful clinically. There are other analytes in the urine that are underappreciated.

Keri, what are your reflections on this discussion? Three or four percent sounds like a great attainment in urinalysis. There are many laboratories that would not be able to achieve such a low rate of manual review.

Dr. Donaldson (Solvd Health): The whole point of decreasing the percent of samples when there is need for a manual review is it gives folks who may or may not be skilled in the art of urinalysis additional time to focus on the samples that need the most attention, and I think these newer instruments make the lower review rates attainable.

What's also inherent in that number is the majority of the samples are classified appropriately and quickly, and meaningful results are returned to the clinician. The fact that that number is coming down and is reproducible and able to be put in other people's hands, from large centralized laboratories to smaller satellite laboratories, and standardized or harmonized across different sites, is a great thing.

To echo what Matt and Jason said, as this standardized data becomes more recognized, you will have additional data points, whether those are prognostic data points in terms of the presence or absence of different types of diseases and if that would change patient care, or flow cytometric results. You can talk about what types of bacteria are present and maybe even about early decisions on antibiotics. That's the bleeding edge, if you will, of urinalysis—if you can get a urine result quickly before a culture result or a susceptibility result comes back. If you can have information sooner and make a better decision, then it can better impact patient care.

Dr. Donaldson

How does your expertise in urinalysis and developing advanced analyzers relate to the work you're doing now as CEO of Solvd Health, which develops technologies that identify risk of disease?

Dr. Donaldson (Solvd Health): It's all how you think about using data being generated from diagnostic tests to drive clinical decisions and eventually enable better patient care. From a method perspective, I'm an agnostic; I don't care where the data comes from or how it's generated. In urinalysis we're talking about different types of information, whether it's visual, image processing, or flow cytometric analysis.

With the work now at Solvd Health, the data source has changed. Instead of looking at flow cytometric analysis, we may be processing data from metagenomic analysis in bacterial colonies from the colon to detect early signs of lesions that could become cancerous. These are still data points. There may be more of them, and one could argue they may be more complex, but we process that data and look at it the same way, and at the end of the day there's a patient and you're trying to inform decisions around that patient's care. As an example, we are part of a consortium using luminal microbiome data to improve the sensitivity of detecting advanced adenomas from 42 percent using tests that use traditional data modeling to more than 90 percent.

Some of our other testing identifies increased risk of developing opioid addiction for prescribing decisions.

Talk about urine as a specimen as it enables some of that work—is it a good or a bad specimen?

Dr. Donaldson (Solvd Health): It's one of the oldest specimens for diagnostic testing. The information the new analyzers are producing allows us to look deeper in urine for additional data points. The most interesting from my perspective would be trying to make decisions—once the urine is positive or negative—on therapeutic selection, in particular with multidrug-resistant bacteria and decreasing the broader coverage as soon as possible, which has

shown to be advantageous. Analyzers are getting closer to having that information available.

One of the most common reasons a person is put on antibiotics is for urinary tract infections. And the difference in days between a urine and culture result is maybe two to three. You take a two- to three-day difference in terms of antibiotic prescription or narrowing it from broad to narrow spectrum, that's a lot of different antibiotics being given to people when you could narrow the resistance profile pretty quickly.

People at Beckman Coulter and Sysmex, to my knowledge, are moving down that same track of saying we can get to earlier detection and stewardship of antibiotics.
Dr. Donaldson (Solvd Health): Quite a few people I know are looking at it. I would encourage it.

Megan, does this sound intriguing as something you look to have on hand in the future at your laboratory?
Dr. Nakashima (Cleveland Clinic): From a systems perspective, yes. I am not involved in microbiology, but all the points Dr. Donaldson spoke to are what we strive toward as a health care system.

Megan, in our discussion last year you said tube manufacturers could do an enormous service if there were preservatives in all urine tubes. Matt, you had comments about how difficult that is. Like a lot of great ideas, the execution is not simple. Has anything come down the track to make it easier to provide preservatives?
Dr. Rhyner (Beckman Coulter): It continues to be a challenge. First, there are not many preservative tubes on the market. There are stringent CLSI guidelines on running urine samples within a specified time frame unless it's in a preservative tube. There are questions, too, on the chemistry side more so than with microscopy about what effect preservatives might have, especially with semiquantitative chemistry strips. It's a continuing topic of conversation.

We have preservative tube claims with the Arkray system, but it is something we will have to address as we look into future developments of new chemistry systems. Understanding better the interaction of the chemical preservatives with the color-changing pad on the strip is an area that merits investigation.

Dr. Nakashima

Megan, have you seen improvement in the availability of good collection tubes with preservatives?
Dr. Nakashima (Cleveland Clinic): We've been doing the majority of our sample in preservative for a while, and that's why it was an issue for me. FDA approval was the big issue because you have to make it a laboratory-developed test when you're using an unapproved sample type. At this hospital we have the resources to do that type of validation, whereas at some of our smaller sites, they don't have the manpower or it's difficult for them to get the manpower together to do that type of study in addition to the usual FDA-approved analyzer validation.

Just to underscore for our readers, in the interest of our industry representatives here, they cannot help with LDTs. That has to remain at the laboratory level for legal and regulatory reasons.

Megan, how have your volumes in urinalysis changed in the last year or so, if at all?
Dr. Nakashima (Cleveland Clinic): In the beginning we had a dip, but since then most of our volumes have been back to normal.

Jason, what are you hearing from your customers in terms of volumes?
Jason Anderson (Sysmex): Our customers did see dips initially, but those volumes are back to pre-COVID levels in a

lot of cases. We have customers who, based on staffing challenges and increased workloads in urinalysis, want to automate and get away from the subjectivity of and time required for those manual, hands-on processes, so we're seeing an increased interest in our automated urinalysis solutions.

Matt, same question to you and, in particular, I would like a comment about people in lower-volume labs and their interest in and appetite for greater automation in urinalysis.
Dr. Rhyner (Beckman Coulter): For the labs, getting back to normal happened a while ago. For our business, it's been that way most of 2021. Starting in late winter or early spring, testing volumes spiked and have been strong ever since.

The budgetary, workflow, and workload concerns in labs are driving the desire for more automation or more efficient processes that require less interaction with the machines. It comes down to a cost-benefit analysis of how much the automation will cost versus the number of samples run. Beckman Coulter just released the DxA 5000 Fit, which is designed for mid- and smaller-volume labs to offer them automation features seen more commonly on analyzers made for higher volumes. That's where it becomes a financial consideration—balancing workload and sample volume and the capital investment to get more automation.

Since the first of this year, the staffing issue in laboratories has become acute. Megan, are you facing some of those same problems in your practice?
Dr. Nakashima (Cleveland Clinic): Yes, we're like everyone else. At the beginning, we had to shift resources, including personnel, into COVID testing. That has flexed back, but we're still dealing with those same challenges and trying to train as many new medical laboratory scientists as we can and to get young people excited in the field. Also, a lab that's doing a lot of automated urinalysis is frequently a 24-hour-type lab, and you have a lot of attrition and turnover in some of those off shifts. That's always been an issue.

Is it your opinion that automation will come to save the day? Or are we approaching an era in the lab where the shortage cannot be answered by anything—whether it's more money for technologists and technicians or more automation? Are we at that crisis level yet?
Dr. Nakashima (Cleveland Clinic): I think there are different ways to flex that. If you have a really small site, then hand-dip your urine if you have to. Other people are going to the other extreme and consolidating practices over four states. There are different ways to approach this problem depending on what type of situation you're in. We're not breaking quite yet.

Anderson

Jason, are you hearing a lot from customers about the staffing challenges?
Jason Anderson (Sysmex): Absolutely. The aging of staff, the lack of highly trained staff, the use of traveling technologists who may not be as familiar initially with lab processes and instrumentation—these exacerbate the challenges.

At Sysmex, we recognize that with our urinalysis solution, simple things like having software that's similar to that of our hematology instruments, which are widely used in the field, can shorten training times and learning curves so techs can quickly become proficient and productive on our system. Sysmex has introduced the TH-11, an optional integrated automatic urine tube decapper—a first in urinalysis. The TH-11 eliminates the nonvalue-added manual process of removing caps and minimizes repetitive stress and biohazard exposure risks to lab personnel. For labs with staffing challenges, the UN-Series is a game changer—tubes are loaded on the system and staff can walk away to complete other critical lab tasks and return to review only those samples that require further

subclassification.

Matt, I'm sure this is resonating with your customers and potential customers.
Dr. Rhyner (Beckman Coulter): Yes, demand for all of our products has been extremely high since the pandemic. Customers have started to see the value for all the reasons we've addressed, in urinalysis, hematology, lab automation, chemistry, immunoassay, and in clinical informatics. Compensation increases are part of the solution, but we as manufacturers also have to make new products for the new reality in which labs exist. Fewer and fewer people are entering the field.

Dr. Nakashima (Cleveland Clinic): Increased demand during the pandemic has been mentioned, but I have experienced and heard people talk about the fact that you can't get capital to buy an instrument right now. Are people buying instruments or are they reaching out and doing exploratory questioning?

Dr. Rhyner (Beckman Coulter): We've seen orders increase. A lot of institutions ended up with extra capital that they're trying to burn off, either through government assistance or reduced costs through the pandemic; that's been our experience.

Jason, would you like to comment on that demand and the availability of capital?
Jason Anderson (Sysmex): We have seen a lot of demand for urinalysis equipment. Every month it seems to be increasing, so there's capital available to labs. Whether they're reallocating it from other needs, they're coming up with that money and are able to secure the automation, especially in urinalysis and hematology, from the Sysmex perspective.

I will close with questions around data handling and the nuts and bolts of IT in urinalysis. Matt, are you satisfied with the level of software and middleware support and reporting of urinalysis data into EHRs for Beckman Coulter users?
Dr. Rhyner (Beckman Coulter): With the release of the DxU Iris, we added several new clinical informatics tools, one of which is ProService, which allows remote monitoring of the instruments for the first time on our platforms. We do offer the Remisol Advance platform for middleware.

As I said, our analyzers produce more information than doctors will perhaps use. I've spoken to several MDs, particularly about sediment analysis, where a lot of information is produced about different particle subtypes, and they might look at only two or three of them or only if there's an abnormal chemistry correlate, for example. What we have today is more than adequate for the clinical information derived. There could always be more, depending on where the field goes, but all the parameters we report are easily available in the middleware.

Megan, how satisfied are you with the IT hook-up to and from your urinalysis laboratory?
Dr. Nakashima (Cleveland Clinic): I think it's good—I hear no complaints from my laboratories.

Touching on what Dr. Rhyner brought up about the amount of information we get for particles, and I discussed this with Mr. Anderson at AACC—I think there's a shift now in what laboratory technologists are trained or competent to do in terms of picking out the billion different types of particles and knowing how clinically useful they are or if we need to quantify, semiquantitate, fully quantitate those things. In my experience with asking some of my colleagues in the clinical sector, the responses vary immensely. Some people say they could not possibly live without X and other people say they don't know what X is.

Keri, do you want to comment on this last question?
Dr. Donaldson (Solvd Health): I experienced this a few years ago when I ran a lab that did urinalysis. We moved from a manual-based to an automated system, and we had to correlate historic reported results to new data that had more granularity, making sure the granularity not only mapped appropriately, which is part of the instrumentation verification, but also that the clinicians understood the granularity and could make decisions from it.

What Dr. Rhyner and Dr. Nakashima are saying is part and parcel to being a good laboratorian—making sure the

information the lab is putting out is used in a way that makes a clinical impact. That's a challenge as you change practice, but there is opportunity—for different types of sediment analysis and flow cytometric analysis. I often use a crawl before you walk, walk before you run analogy. With urinalysis particulate analysis and being able to distinguish things we couldn't before, we're still in that crawling phase because we have to put it in front of folks and make sure they understand it before they can walk and make a decision or eventually run and improve patient care.

Matt and Jason, would you like to make a closing comment?

Dr. Rhyner (Beckman Coulter): We're excited by the response to the DxU Iris launch at AACC; it's been overwhelmingly positive. The early adopters are happy, and it makes me proud that the team worked on the project throughout the pandemic and hit the product launch at AACC.

We are investing in the area and will bring new products to the market that are clinically and workflow differentiated. The next few years in urinalysis will be an exciting time.

Jason Anderson (Sysmex): We're proud to offer a robust, accurate, and efficient urinalysis solution that can be configured and scaled to meet the needs of different sized labs. For labs that want to fully automate and standardize their urinalysis testing process at the highest levels, the UN-Series can facilitate this through a combination of technologies and capabilities.

As Dr. Nakashima said, the full power of fluorescent flow cytometry has not been tapped. There's a lot to look forward to in the discipline of urinalysis. There is a continuing need to take a closer look at best practices and the expansion of the clinical utility of urine particles and parameter detection and measurement. We look forward to continuing our work with customers to enhance our understanding as well as participate in urinalysis best practices evolution.

Keri, a final comment from you.

Dr. Donaldson (Solvd Health): Increased standardization is important, and having scalability to different laboratories and harmonization are some of the strengths these companies have been working on. I would advocate, Matt and Jason, that as you're looking at additional pieces of information, always keep it patient-centric because at the end of the day, the information that's being provided is used to steer patient care. When a urine sample is positive, defining what is there and what the appropriate clinical decision could be—this is the next five to 10 years of this analyte.

And Megan, what are your final thoughts?

Dr. Nakashima (Cleveland Clinic): It is an exciting time for urine. There has not been movement in the field for a while and we're getting more interest. People are not only seeing the advantages we can have clinically and diagnostically but also workflow-wise. The new partnerships that have been made especially in the past couple of years are really interesting.