In hematology, making the most of automated solutions

October 2023—Hematology analyzers and the related workflow, expertise, efficiency, and IT matters were the topic of a roundtable when CAP TODAY *publisher Bob McGonnagle met online Aug. 29 with two pathologists and representatives from Horiba, Siemens, Sysmex, CellaVision, Sight, and Abbott. Their conversation follows. Click here for* CAP TODAY's *guide to hematology analyzers.*

Dr. Chaves

Fernando Chaves, what are the advances in artificial intelligence in the field of hematology, particularly automated hematology, since we spoke during our roundtable at this time last year?
Fernando Chaves, MD, global head of hematology, Siemens Healthineers: Technology now enables full-field digital morphology, a full image of the entire slide scan. Now we can do with hematology what has been done for over a decade in surgical pathology. It brings benefits to customers because it not only preclassifies cells and facilitates the technologist's work but also enables full remote consultation.

Having digital images under a full slide context creates an opportunity for clinical innovations. It's already happening with applications for reviewing bone marrows and interpreting morphological abnormalities in the blood, and it could also be done in the future through automation and artificial intelligence solutions. Some of the sepsis parameters that are based on hematology are primarily morphologic parameters that are identified through a histogram. Now we have more sensitive technology that can identify abnormalities such as granularity of cells and heterogeneity of volume. All of that is because images are now digital and can be quantitatively analyzed through artificial intelligence image analysis algorithms.

Jonathan Galeotti, for years we've hypothesized that there's more to be learned from studying the cells than we've been able to realize. Now we seem to be on the brink of breaking through in several important areas. Fernando mentioned sepsis but there's also a plethora of hematologic malignancies that we may be able to understand better. How are you dealing with this at the clinical level in your institution at Chapel Hill?
Jonathan Galeotti, MD, clinical assistant professor, Department of Pathology and Laboratory Medicine, Division of Hematopathology, University of North Carolina School of Medicine: As the field moves forward, it takes a little time for it to work its way through academic labs and into clinical practice. We're on the front end and have not yet incorporated it much into our hematology practice. There is certainly a need—we still have staffing issues. Anything you can do to streamline the process, to make review and autoverification easier, is on our minds all the time. Hope is there, but we haven't realized it yet.

Tim Skelton, a lot of this requires a healthy IT backbone. Tell us how the IT environment at Beth Israel Lahey Health is being either friendly or frustrating as you look to bring in these latest applications in hematology.
Timothy Skelton, MD, PhD, medical director, core laboratory and clinical informatics, Lahey Hospital and Medical Center, and medical director, laboratory and pathology informatics, Beth Israel Lahey Health: We're a 13-hospital system and we're all standardizing to a single electronic health record. We're struggling with where some of these algorithms should live. It's a little different than the hype about artificial intelligence; we've been focusing on incorporating expertise. We do that by building into the algorithms within our IT systems the knowledge of our best

hematology medical technologists. We're doing this so that on the off-shift at a remote community hospital or a hematology-oncology lab, for example, the information based on this knowledge pops up for a technologist who may be a traveler or isn't that experienced and tells them what the findings are, interprets the findings, and informs them of the actions to take. The middleware, instrument IPU [infrastructure processing unit], electronic health record—all are advancing quickly, so we're always working to determine in which IT system we want to build a certain logic.

We use the CellaVision system, so pathologists or experts in the central lab can remote in and interpret if there's a question. Having digital images is better than glass slides. We're not doing anything with full slide imaging in hematology.

Dunbar

Scott Dunbar, it seems as though hematology is going the route of surgical pathology; that is to say, having the ability to remotely view specimens by experts who may be miles away. Do you see that evolution?

Scott Dunbar, director, Americas, CellaVision: More and more people have been buying remote review licenses. A lot of large systems have a hub-and-spoke model where there's a mothership hospital and five to 10 satellite locations and a centralized database server that IT staff can control and lock down so things are encrypted appropriately. But we have pathologists and senior medical technologists remote reviewing into smaller hospitals where there isn't the expertise. We see more people using remote review to improve turnaround times, centralize expertise, and standardize the most subjective area of the laboratory. We won't argue over an 87 glucose on a standard curve in a spectrophotometer, but we could argue all day over what a monocyte in a reactive lymph is. How do you get that expertise? It's a combination of the artificial intelligence we've been discussing here and having qualified morphologists.

Ihab Zidan, what are you doing at Abbott to help capture some of the promise of informatics, machines, and images?

Ihab Zidan, director, global marketing, hematology, Abbott: The biggest need we see in the market is automating labs with sophisticated IT solutions that improve the efficiency of workflows, whether it's because of staff shortages or lack of expertise. We need to account for variations in expertise across the world, and a strong IT system supports not only improving efficiencies but also the algorithms and the clinical decision support element of that with the inclusion of international standards. How can we improve our high-volume lab performance with sophisticated IT elements to help free up human expertise? That is the question we are trying to solve as an organization.

Jill Crist, we've been talking about staffing shortages for a few years now, but the atmosphere at this year's ADLM meeting was one of confidence and optimism about how much more automation could be introduced into the laboratory, which is the key to solving some of the staffing issues. Do you agree?

Jill Crist, senior manager, compact and scalable automation, IVD product marketing, Sysmex America: Yes. There was tremendous activity at the automation line we exhibited at the meeting. We introduced modules that improve automation so that very little technologist time is needed, and CellaVision helps with that. We introduced an automated QC module that attracted a lot of interest. We are seeing more laboratories connecting to total lab automation than we've ever seen, and I think it's a result of the staffing shortages.

So a laboratory that has a smaller volume is a better candidate for TLA now than it might have been three years ago?

Jill Crist (Sysmex): That's right.

Susan Behnke, what are you hearing from your customers and potential customers as you discuss these issues?
Susan Behnke, MT(ASCP), MBA, senior marketing manager, Horiba Medical: Horiba focuses more on near-patient testing—physician office labs and clinics rather than the large hospital market—but the issues are the same. Staff turnover keeps training at a significant level. The question is not only what can be done to automate but also how to keep the new technologists trained.

In addition to training, there is also competency assessment that's required under CLIA. Is that right?
Susan Behnke (Horiba): Exactly. All the hematology analyzers are moderately complex, so there is a competency piece. This provides another avenue for technologists who are interested in doing something different, such as being a consultant to clinics and physician office labs to help keep those facilities competent and reporting out good patient data and results.

Roopra

Bob Roopra, tell us how Sight Diagnostics plays within this constellation of the vendors and clinical needs we have.
Bob Roopra, chief commercial officer, Sight Diagnostics: We're an AI-based hematology platform that performs CBC tests in decentralized settings. Our technology is based on digital live cell monolayer imaging, so the results are based on the ground truth of CBC—a flat layer of blood cells under a microscope. As we see it, the digital space is about the confidence it gives you and the quality of the results—no compromised performance in decentralized settings is what we're about. Laboratories are about transportation, sampling, a sample being badly hemolyzed and having to be repeated, patients who sit around and miss an opportunity. How do we connect those dots? Sight Diagnostics has found its space in those meaningful places and is giving laboratories the ability to expand outside the four walls. You need good governance that covers the IT and maintains control of the operators. Those clinics and spaces that Susan talked about are where Sight is coming into its own. We're seeing growth in many markets around the world, including the U.S., and in hospitals that are going to a hub-and-spoke model. We're even seeing a departmental hub-and-spoke effect starting to take place; that's new to us.

Nitsan Maayan-Rabinowich, point-of-care testing technology had a strong presence at the ADLM meeting. Part of that is a repurposing of devices coming out of the pandemic but also because we are going to large health systems and to hub and spoke. Do you have the same impression of the way the market is moving?
Nitsan Maayan-Rabinowich, chief strategy officer, Sight Diagnostics: We are seeing decentralized diagnostics in acute care within hospitals and the prehospital settings. When a health care system becomes more loaded, the need for decentralized labs grows, especially for acute-care settings, such as freestanding EDs, urgent cares, critical access hospitals, and even emergency departments within general hospitals.

We understand there is a staffing shortage, so with our live cell monolayer imaging technology we aim to reduce the need for additional smear reviews. This goal is always important, but it's even more important in decentralized settings where you usually don't have the expertise required for smear reviews but still want and need to make good clinical decisions, especially for patients with acute and severe clinical conditions. This is where Sight fits in.

Jonathan Galeotti, we understand that clinicians, nurse practitioners, and others have a need for explanation and reassurance of the results they're seeing regardless of how and where they're seeing

them. Is there an increase in the need for consults, the need to explain hematology results?
Dr. Galeotti (UNC School of Medicine): Yes. We have seen an increase in requests to review even what is reported as a normal result on an automated analyzer. People want reassurance or they have a question about the result and want to confirm it.

Dr. Skelton

Tim Skelton, same question.
Dr. Skelton (Beth Israel Lahey Health): Absolutely. When I'm on call and doing clinical consultation, the questions are getting more basic. There are more people practicing at the top of their license—more physician assistants, nurse practitioners, first-year residents, or hospitalists are handling things. I try to identify those questions through the consultation service and also build decision support into the electronic health record—not in the laboratory but out in the clinic. It is productive and helps bring value-based health care into the field. The biggest financial impact of the hematology lab is the information and what it causes clinicians to do differently based on the results and timing of the results.

The other tool we have in the integrated electronic health record is the business intelligence. We can use the analytic tools and reports to figure out what reality is. Often people would report things and then reality is different when you get the data that tells what the providers, nurses, and doctors are doing when they get the information. Business intelligence reveals a big gap, and we build decision support tools to close the gap.

How specifically are you doing decision support? Where does it live in Beth Israel Lahey Health?
Dr. Skelton (Beth Israel Lahey Health): It lives in the electronic health record. We have one database that has all the laboratory and clinical information. I'm board certified in clinical informatics, and we look at clinical informatics as the practice of medicine; it isn't something a computer analyst can do. It is driven by the MDs who have gone to physician-builder training for the EHR, and we know how to build it. We don't often do the build ourselves but we'll direct the computer analyst to build it and then we'll validate it and look in the various systems to make sure the build is going appropriately. We start with the report of what's happening and then after we build the decision support, we go back to the report and we can see the practices changing and improving. The goal is to change clinical practice based on the information the hematology analyzers are generating.

Many CAP TODAY readers will be wondering how to get such perfect capture of laboratory data into EHR systems. It's one of the headaches we all have to live with, isn't it?
Dr. Skelton (Beth Israel Lahey Health): Yes. One of the roles for clinical informatics is to have a standard for the institution that the data going in is good data.

A lot of the intervention involves capturing the data differently so the data in the database is accurate, validating the capture of data, running reports to find gaps in the accuracy of the data, and looking at what actions are being taken as a result of the data.

Jill Crist, can you comment on the importance of having specific reference ranges for the patient population we're applying these reports to?
Jill Crist (Sysmex): Our customers always request reference ranges, and we typically suggest they do studies to create their own reference ranges. We have established reference ranges in our instructions for use, but I've had physician requests for reference ranges for people who are transgender or transsexual, and we frequently have requests for reference ranges for pediatric and neonatology patients. For pediatrics and neonatology, we've partnered with several physicians at large systems.

Fernando Chaves, can you comment on the issue of reference ranges? It seems that without well-thought-out and well-established reference ranges for patient populations, much of the work we do interpretively or in AI may be misleading. In other words, if we're going to feed the AI, we need to do so with the best, most pristine reference ranges for the patient.

Dr. Chaves (Siemens Healthineers): All the AI algorithms and solutions that go in that space open a vast array of opportunity for going to personalized health care. Then you can cut the data any way you want. Because we have the technology now that enables us to capture and analyze the data much more efficiently than in the past, we can understand what is normal for different groups and what is abnormal. Reference ranges are an essential part of enabling all the solutions we have been envisioning here.

Bob Roopra, how do you control for reference ranges with your application? I'm assuming you have a vast number of users from different populations and places.

Bob Roopra (Sight Dx): We have eight age- and sex-related default ranges within the device, all of which can be selected. For reference range validation, local health care providers are advised to conduct studies on their own patient populations.

The biggest challenge we've had in the past 30 or 40 years is the way the populations have changed not just with growth within a population but also because of migratory effects. In hematology there should be best practices around setting and understanding what's normal in your own backyard. Maybe with AI there's a tool that can be used rapidly in the lab to define those ranges for each place.

The most interesting samples, for that matter, are the ones with poor results that get referenced and end up requiring film review, which you can see in patients with severe clinical conditions. They're the most interesting because they start to bend the rates of what we call normal, and normal is limited to the technology. So we're pushing the boundaries on that because we're looking at it differently. It's an interesting space to look at and should be taken seriously

Zidan

Ihab Zidan, have you found an improvement in the percentage of manual differentials your laboratory customers are performing by virtue of their better understanding and better use of the automated results?

Ihab Zidan (Abbott): We are seeing more dependence on the technology these analyzers offer. Review rate is a major determining factor for labs when considering new analyzers. Looking deeper into scatterplots and scattergrams, which are often overlooked, can provide a better picture for the user and can impact review rates. Because certain parameters do not appear the same way or are not measured the same way across analyzers, that can create confusion among users, especially if you're not looking at the same system or the same technology within the health system. Standardized technologies coupled with the increased adoption of digital morphology, AI, and clinical decision support can help reduce the percentage of manual differentials.

Susan Behnke, does Horiba set a goal or an ideal of a percentage of manual differentials that you would expect your users to have to perform?

Susan Behnke (Horiba): Not specifically because it depends on the patient population of a practice. The manual differential rate for an analyzer in an oncology practice will be different than the rate in a general practice. But with the technology analyzers utilize to perform the differential, including mobile thresholds, cell differential is excellent. The cells are placed into the correct location on the matrix. Most practices can keep it below 10 percent.

Dr. Galeotti

Jonathan Galeotti, do you have a benchmark in your mind for your patient population for manual differentials? I realize it's an easy and yet impossible question.
Dr. Galeotti (UNC School of Medicine): We are a large academic hospital with many affiliates that send us things to review, so our patient population is varied and we see more from our oncology patients. There are also challenges with autoverifying differentials from our ICU patients; we review a lot of those. Our goal is to minimize the ones that don't need a manual review. There are many that a pathologist must look at, but it would be ideal to eliminate the ones that could be autoverified or not get normal ones that have been flagged for incorrect reasons or should not have been flagged.

Jill Crist, what should our readers know as of 2023 about manual differential rates?
Jill Crist (Sysmex): The key is trusting the technology of the instruments. The smaller community hospitals may be less trusting of an automated differential. The more advanced places tend to be more accepting of the automated differential because they understand the technology and have abnormal populations they can learn from. With the exclusion of commercial reference labs and oncology and pediatric populations, the overall autovalidation rate is around 85 percent. With staff shortages and more and more sick patients, people need to embrace their automation and technology.

Tim Skelton, you're in a large, diverse system—if you had a policy statement on the manual differential, what would it open with?
Dr. Skelton (Beth Israel Lahey Health): Recently the biggest gains we've had in reducing manual differentials are from using the CBC and absolute neutrophil count instead of the CBC and diff. There are fewer instrument flags that require manual review on an absolute neutrophil count than there are on the manual diff. By working with the clinicians and saying maybe you just need a CBC and absolute neutrophil count here, we've seen an uptake in the use of that test order rather than the CBC and diff. For our very sick inpatients, our bone marrow and liver transplant patients, patients on chemotherapy, and also for screening for sepsis, we use the CBC and absolute neutrophil count instead of the CBC and diff. And like Jill said, you need to understand the technology and push it to its limits. The time to test what the instrument is capable of and optimize the auto-reporting of the differential is when you bring in a new instrument.

Dr. Galeotti (UNC School of Medicine): We did something similar where we limited the number of manual differentials for individual patients. If a patient had a manual diff within 24 hours, we wouldn't do another one unless there was an urgent need to repeat it.

Jill Crist (Sysmex): I'd like to ask Drs. Skelton and Galeotti—pediatricians and neonatologists tend not to want to go with automated differentials and instead prefer manual diffs. Do you also see that and, if so, do you see it changing? How can we get these physicians to embrace and accept the automated diff? Or will it always be a challenge?

Dr. Skelton (Beth Israel Lahey Health): The issue is the band count. Automated instruments cannot tell the difference between a band and a segmented neutrophil but technologists can, or believe they can. There's a huge variation. The skill of the medical technologist will affect the band count. Also, it's subjective: What's a band and what's a segmented neutrophil? The neonatologists have not given it up; they want a band count. And the neonatologists' professional literature supports that.

From a pathology point of view, the band count is not precise or robust enough. And the automated instruments can't do it, so if I had my way I would lump the bands and the segmented neutrophils together. But we don't get

buy-in from the neonatologists on that.

Dr. Galeotti (UNC School of Medicine): Similar answer—they're not going to give it up. Most of those currently do not make it to the pathologist; they are reviewed by our technologists. I do worry about that as we lose our senior technologists. It's going to be a bigger problem.

Dr. Chaves (Siemens Healthineers): As far as in the industry, we see two sides of the story. There is a pressure to lower the manual counts because of staffing challenges. At the same time, if it is easier to process manual slide reviews through digital morphology and automated solutions that facilitate the interpretation of the images, maybe the conversation will shift from the percentage of differentials to how difficult it is to process and obtain reliable information from those novel tools. If it's easy and automated to review a differential, we could even have higher diff counts and that would not be much of an issue.

Scott Dunbar, where do you think the CellaVision application will be in the next few years and how will it continue to enhance the field? What's in your pipeline?
Scott Dunbar (CellaVision): It's always important to add more assays, more offerings to tedious tests in the laboratory, whether for bone marrows, which are coming out shortly, or for more esoteric things like Kleihauer testing, which is tedious because when you say something is positive, it might be 1.4 percent. For a remote laboratory that doesn't have a person who is good at Gram stains, it would be wonderful to put Gram stains and other assays on that could be read by a microbiologist at a mothership.

Band counts and standardization are hard. I'm in laboratories every day and medical technologists will not agree on a cell. I can show five cells on a screen and everyone will call them something different, and if you look at Rumke's table of variability, everyone is right or wrong. Someone once asked me, How do you become a better morphologist? You could easily say, Do more differentials. But if you have a bias, you become a more consistent morphologist, not a better one. The only way to become better is from coaching, having someone give you input to help you become a better morphologist—not by doing more differentials.

Bob Roopra (Sight Dx): I'd like to make a point about the effect on manual diffs. In oncology we have had an impact on how many samples get sent back to the lab, fundamentally because the way our CBC solution works is essentially as an automated smear with AI. By nature AI is consistent and not prone to a specific morphologist interpretation, as the system is trained on extensive amounts of blood samples and getting better and better through R&D improvements, and it has affected how many patient results end up requiring manual differentials. So eventually, AI has the potential to make the answers better and better.

Maayan-Rabinowich

Nitsan Maayan-Rabinowich, tell us what's ahead in the next two years for Sight.
Nitsan Maayan-Rabinowich (Sight Dx): At Sight we skipped the stage of going from manual review to digital review and went directly to AI-based CBC digital imaging processing, which will eventually reduce the need for further blood smear reviews of any kind. On top of that, we see a trend going from hematology to cell morphology, and this is exactly what our platform is about. Our name, Sight Diagnostics, means we aim to diagnose everything you can see in a blood sample. We started with malaria, continued to CBC, and now we're working on additional applications with the same core technology. These applications will solve big challenges for clinicians and patients.

Jill Crist, what are one or two things in Sysmex's pipeline in the next couple of years?

Jill Crist (Sysmex): We have a lot of big data and we're working on things with AI and continuing to bring automation to the laboratory. We recently released three modules that have helped with that, and there will be others. We're going to move with the industry.

Susan Behnke, same question.
Susan Behnke (Horiba): We have a next-generation hematology analyzer, which is available outside the United States, that includes flagging for infectious diseases such as malaria and dengue.

Tim Skelton, what one thing could industry do to make your life a little easier?
Dr. Skelton (Beth Israel Lahey Health): Critical value calls. With the advances in IT, a lot of the providers already have the information before the laboratory calls. In the OR the anesthesiologists have a screen, and the inpatient nursing area has a track board that pops up the critical values and they have already acted on it by the time they get called. We've reviewed and cut back a lot on the critical value calls in hematology. We only call things like the platelet count, white count, and the absolute neutrophil count the first time it's critical, per encounter. The real-time push delivery of results has enabled that.

Jonathan Galeotti, what is the one thing for you?
Dr. Galeotti (UNC School of Medicine): The ability to review remotely, full slide imaging, all the things that streamline workflows and make it easier for pathologists to get their hands on slides and maximize the efficiency of things that are going to happen regardless of the technology we're using.

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