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Diagnosing the Disconnect

Brain drain, diagnostic inaccessibility, and their effect on global health

12

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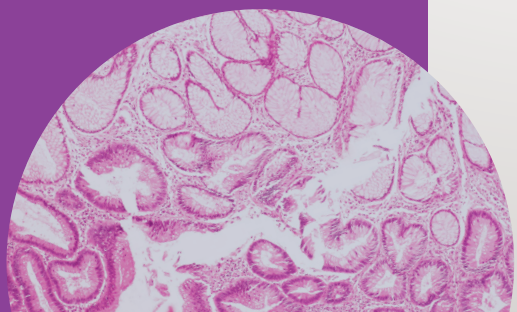

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Breathing More Easily, With Biomarkers

When traditional diagnostics fall short, biomarker testing offers respiratory relief in resource-limited settings

Despite the importance of standardized diagnostics, there are areas across the world that do not and cannot abide by regulated processes (1). In low- and middle-income countries (LMICs), this can be for a multitude of reasons: lack of resources, limited training, and high costs are just a few examples.

Respiratory diagnostics is just one area where systems are lacking. As a mild asthma patient, I'm well accustomed to spirometry and peak flow tests to check the progression of my condition. But for individuals in LMICs, this isn't a regular opportunity. In 2023, researchers found that 95 percent of chronic obstructive pulmonary disease cases they identified were previously undiagnosed (2), and even when available, maintenance treatments were unaffordable.

Of course, SARS-CoV-2 had a significant effect on the world as a whole, but its damage was further exacerbated in LMICs – taking attention away from lower respiratory tract infections that are common causes of mortality in children (3), and further preventing improved patient care.

In this issue, we speak with professionals working in LMICs to identify the key unmet needs in respiratory diagnostics, and the opportunities presented with biomarker testing. Are C-reactive protein tests the path forward in respiratory diagnostics in LMICs? What role does point-of-care testing play in advancing patient care? And how do we make standardization accessible worldwide? Join the conversation: *edit@thepathologist.com*

Jessica Allerton,
Deputy Editor

See references online

Feel free to contact any one of us:
first.lastname@conexiant.com

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Change of address: info@thepathologist.com
Julie Wheeler, The Pathologist, Texere Publishing Limited, Booths Park 1, Chelford Road, Knutsford, Cheshire, WA16 8GS, UK

General enquiries:
www.conexiant.com |
info@thepathologist.com
+44 (0) 1565 745 200 | sales@conexiant.com

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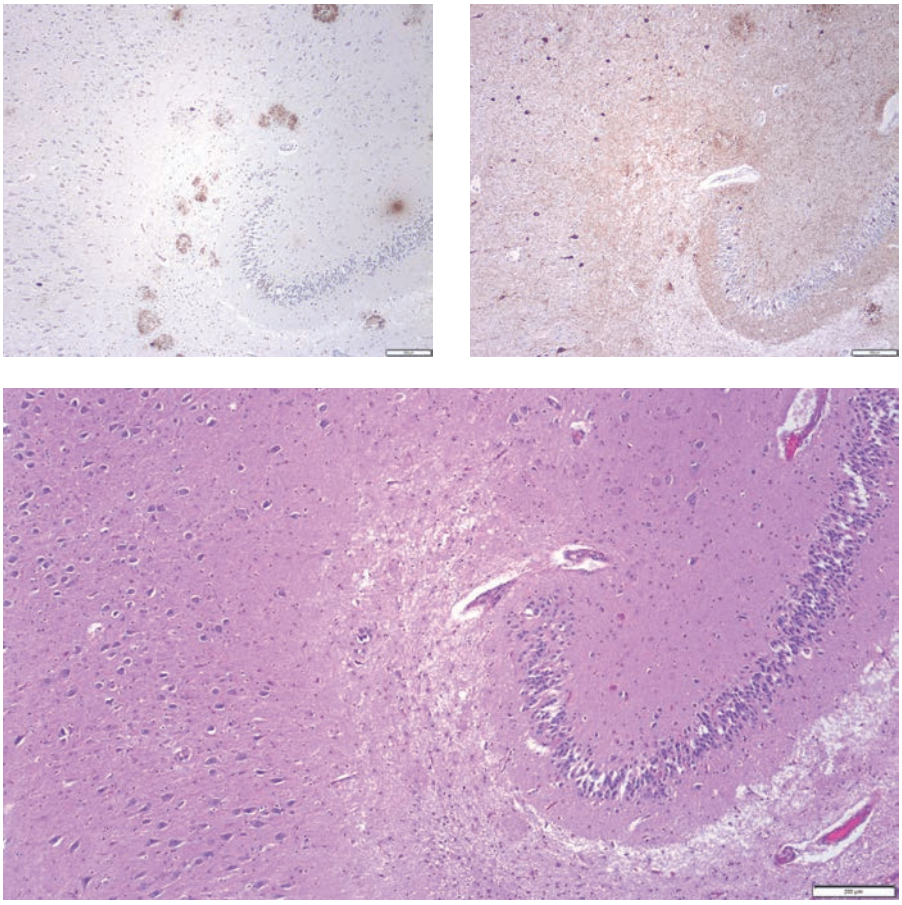
Rethinking "Asymptomatic" in Brain Autopsies

Unexpected changes in "control" brains calls attention to underrepresentation in Alzheimer's research



The majority of neurodegenerative research is conducted in non-Hispanic White participants – removing a large subset of racial groups despite the prevalence of dementia. In response, a group of researchers in Houston Texas, US, aimed to improve understanding of dementia-related findings in asymptomatic African-American populations. We spoke with the team to check in on their progress and what they've discovered so far.

What inspired this research?
We have a brain bank collecting specimens with different health conditions, including control brains for research. We noticed that some "control brains" had unnoticed neurodegenerative changes and decided to screen all brains collected for neurodegenerative status, allowing for more accurate group profiling for future studies.

Can you describe the inclusion criteria for the autopsy cases?
Each autopsy brain came with a clinical history. If there was no recorded history of memory issues or movement disorders, the brain was labelled as "asymptomatic". Of course, each autopsy had a cause of death, more commonly from cardiopulmonary conditions.

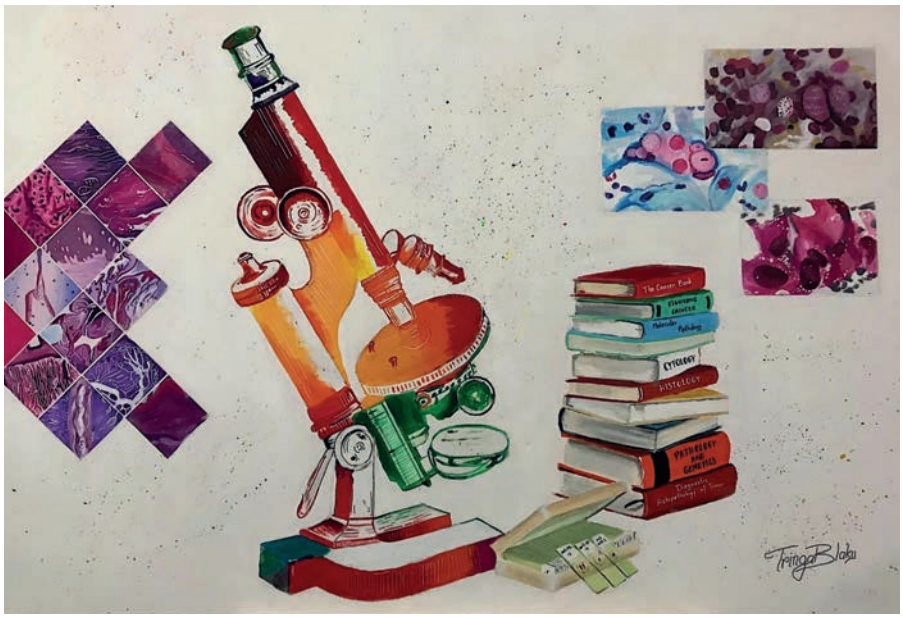
What have been your main findings so far?
We found signs of neurodegeneration at various stages in the brains of asymptomatic patients. Surprisingly, the percentage was quite high. However, since our screening is still in the early phases, we don't yet have enough cases to make strong statistical comparisons with published data.

Have you come across any challenges during your research?
It's a very interesting project, but we still need more cases for analysis – particularly in different ethnic groups, including African-American, Hispanic, and Asian. We currently have very limited data from some of these populations compared with Caucasian cases.

What are the implications of your findings for early screening or preventive strategies, particularly in African-American populations?
In the past, we only used the neurodegenerative panel on cases with a clinical diagnosis like Alzheimer's or clear signs under the microscope, such as plaques. Now, we're screening all brains, without focusing on any one ethnic group. This gives us a better overall picture of the different types and stages of neurodegenerative changes in the general brain bank.

We're also working to gather related clinical information. This is just the start of a larger project, and we hope to have answers to your question as it progresses.

What do these results mean for our understanding of Alzheimer's disease?
The brain changes seen in Alzheimer's disease are very diverse and may be influenced by genetics, health, and lifestyle. Right now, we've only just begun to explore a very complex issue – there's still a lot of work to do before we can fully understand what the future holds.



Cellular Essence of Pathology

Our image of the month highlights the beauty in cellular analysis

Our image of the month comes from Selamete Çeku, who says "My #pathart reflects the essence of the pathologist's profession – a commitment to transforming the future of healthcare. In the 21st century, cellular analysis must evolve through the application of digital pathology. By integrating algorithms and AI into diagnostic workflows, we lay the foundation for the advancement of precision medicine – bringing more accurate, personalized, and efficient patient care."

Credit: Selamete Çeku, Anatomic Pathologist, Institute of Pathology, University of Prishtina, Republic of Kosovo

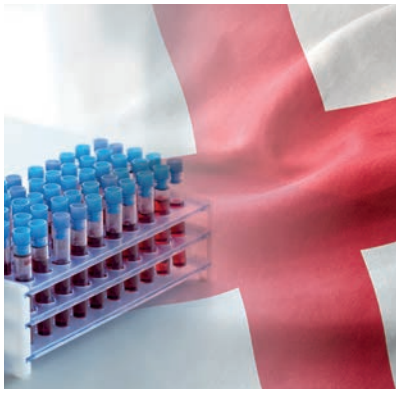
QUOTE *of the month*

"Whatever it takes to get the most accurate diagnosis is worth it – because everything that follows depends on it."

Daniel Brat (See page 26)

UK Liquid Biopsy Rollout

National Health Service (NHS) launches world-first blood test approach for faster lung and breast cancer treatment



Credit: Adobe Stock (Edited)

NHS England has announced that liquid biopsies are now routinely available for eligible patients with lung and advanced breast cancer in NHS hospitals. Thousands of cancer patients in England are set to benefit from the new approach to testing that could accelerate access to targeted therapies – enhancing quality of life and providing personalized care while reducing system burden.

Up to 15,000 lung and 5,000 breast cancer patients each year are expected to benefit from this approach, enabling clinicians to identify genetic mutations and initiate tailored treatment up to 16 days faster than traditional tissue biopsies.

The Royal College of Pathologists praised the move, calling it a transformative step in cancer diagnostics. Looking ahead, the NHS is now considering liquid biopsy use in other cancers, including pancreatic and gallbladder malignancies.

Renal Pathologists: Unsung and Essential

A call to elevate kidney pathology from the margins to the medical mainstream

By Mariia Ivanova, Pathologist from Kyiv, Ukraine, currently residing in Milan, Italy

Renal (or kidney) pathology remains as a somewhat overlooked subspecialty in pathology. While the global research and pharmaceutical industries continue to revolve, rightfully, around oncology – enabling us to whisper, "we fear much less" – chronic kidney disease (CKD) remains in the shadows.

CKD is marked by numerous comorbidities and a wide spectrum of physical and mental complications. Patients with the condition are too often underdiagnosed, pushed to the periphery of basic healthcare, especially where specialized centers are absent. According to the US Centers for Disease Control and Prevention, approximately 14 percent of the US population has CKD – and 9 out of 10 affected individuals are unaware of their condition.

As a renal pathologist, I recall diagnosing renal biopsies with incidental findings of advanced-stage glomerular diseases in patients referred after routine check-ups and urinary abnormalities detection. On this journey in a unique and "niche" subspecialty, I've been fortunate to learn from giants in the field. I invest eagerly in rare and costly renal pathology books and I'm also proud to provide free digital consultations for my father's patients in Ukraine – even from my home in Italy (my father is a "rock star" professor of nephrology back home).

Yet, even among my most brilliant and experienced pathology colleagues, I sometimes feel the absence of a strong nephropathology network – a shoulder to lean on. Accurate diagnosis of glomerulonephritis is vital for treatment decisions, often involving potent therapies that are still frequently overused or underutilized in clinical practice.

And I confess: I struggle with almost every diagnosis. Because even though we typically operate "behind the glass," our responsibility is clear. There is always a human being on the other side. And the things I state in my medical report will bear the consequences to their choice of treatment, healing, and quality of life.

There is more to it: renal pathologists are rare, as mentioned. That said, there is little to no chance a patient's case would be taken to second opinion if I don't do it myself. My errors, if committed, may come at a great cost to a patient, in many senses.

Let's also consider the preanalytical challenges. I've trained as a visiting pathologist in numerous laboratories worldwide. Some institutions are equipped with dialysis and transplant departments, skilled teams, immunofluorescence/immunohistochemistry, and electron microscopy. Sadly, many medical centers worldwide are not endowed with this luxury.

In Kyiv, our lab handles only a few kidney biopsies each week. We don't rely on large commercial labs due to time and cost constraints. We (traditionally) rely on ourselves in manual tissue processing and staining. Still, we remain one of Ukraine's most important referral centers for kidney biopsies, a fact that fills me with pride.

But let's be honest: if not for the war, how quickly would we find a sponsor to buy a portable slide scanner? Who would replenish the antibody supplies? Who would pay a technician for just one or two cases a week? If renal pathology is considered rudimentary in so many European centers, what hope do "developing countries" have?

While our environment inevitably increases DNA damage and the risk of disease, awareness and lifestyle still matter – especially for conditions like obesity, type 2 diabetes, and CKD. We need to focus more on public education around CKD: its risks, signs, and preventive measures.

I would be thrilled to see renal pathology take a more prominent role – both online and in real-world communities. The current outlook is sobering, and our expertise will only become more critical in the years to come.

Specimens Deserve Standards

Defining the roles of grossing personnel is crucial for maintaining diagnostic integrity and protecting patient outcomes

By Jennifer Hudson, Chair of the AAPA Legislative Subcommittee

The gross examination of anatomic specimens is a critical component of pathology, forming the foundation for accurate diagnosis. However, the complexity of grossing means that errors – especially when performed by untrained personnel – can lead to serious consequences for patients.

Historically, grossing was performed exclusively by pathologists and pathology residents. However, as workloads increased, specially trained pathologists' assistants (PAs) were introduced to provide necessary support. PAs complete formal education and training through accredited programs, equipping them with the advanced knowledge required for surgical specimen processing.

Meanwhile, grossing technicians (GTs) have been introduced to support other areas of the pathology lab without the intense training undertaken by PAs. Today, PAs and GTs perform the majority of grossing tasks, raising important questions about the scope of practice, training standards, and regulatory oversight.

The growing shortage of pathologists also presents a significant challenge. Fewer medical students are choosing pathology, and advancements in personalized medicine means pathologists now spend more time reviewing complex cases under the microscope – leaving little time for grossing.

A pathologist once told me, "diagnosis begins at the gross bench." Choosing the right tissue samples is critical; even the most skilled histology staff cannot compensate for poorly sampled tissue. As pathologists' roles shift away from the grossing room, it's more important than ever that those doing the work are properly trained and qualified. Clarification of non-pathologist grossing personnel are essential to ensure patient safety, maintain diagnostic accuracy, and optimize workflow.

Lacking regulatory oversight

Despite the critical role of grossing personnel, regulations remain minimal. The only federal guideline – Clinical Laboratory Improvement Amendments (CLIA) '88 – classifies grossing as high-complexity testing but only requires an associate degree in lab science or medical technology. Only three US states currently license PAs, and the rules vary significantly. California is the only one that has taken initial steps to differentiate PAs from other grossing personnel by establishing a tiered supervision system.

While CLIA-qualified personnel may be adequate for low-complexity cases, such as routine biopsies that don't require dissection, it's concerning that moderate- to high-complexity cases – including cancer resections – aren't more strictly regulated. These cases require an advanced knowledge of pathology. Even routine specimens, like an appendix, can contain unexpected findings that can be overlooked by inadequately trained personnel.

Defining roles

The roles of PAs and GTs need to be clearly defined, with proper education, training, and scopes of practice. The American Association of Pathologists' Assistants (AAPA) has issued a position statement, recommending that GTs are limited to "macroscopic examination of routine biopsies and low-complexity specimens that do not require selective sampling," due to their limited formal education and standardized training.

In contrast, PA accredited programs include in-depth education in pathology, anatomy, and disease processes, plus over 10 months of hands-on-lab experience. PAs not only perform highly complex grossing, but also review patient histories and assist in writing autopsy reports – tasks that were once handled by pathologists. In this way, PAs function as physician extenders, much like nurse practitioners and physician associates.

A recent CAP Today article highlighted improvements in lab efficiency and workflow by utilizing PAs as pathologist extenders. An ideal lab setup would have pathologists focused on microscopic diagnosis, PAs handling moderate to high-complexity grossing and frozen sections, and GTs handling only low-complexity grossing.

Strengthening regulations

To maintain high standards and keep patients safe, the AAPA recommends the following:

- **PAs** should graduate from a National Accrediting Agency for Clinical Laboratory Sciences (NAACLS)-accredited program and pass the ASCP board certification exam. This allows them to hold responsibility for grossing high-complexity specimens that require selective sampling.
- **GTs** should meet CLIA requirements for high-complexity testing personnel, but only work on small routine biopsies and low-complexity specimens where the entire tissue is submitted for microscopic examination without selective sampling.

Licensing or additional regulations could help clearly define the responsibilities of each role. Licensing PAs would enhance lab efficiency, safeguard diagnostic accuracy, and give pathologists greater confidence in delegating grossing tasks – allowing them to focus on microscopic diagnosis.

By formalizing these distinctions, we can ensure the highest standards of patient care while maximizing the skills of all pathology professionals and support attending pathologists, who bear the ultimate responsibility for rendering accurate diagnoses.

Understanding the Journey to the Laboratory Matters More Than Ever

Collaborative study provides a data-driven roadmap for safeguarding the pathology workforce

By E. Blair Holladay, CEO, American Society for Clinical Pathology

Pathologists and laboratory professionals are needed in healthcare now more than ever. Yet, our profession faces a critical workforce challenge. We can better address this challenge if we first understand how people currently in laboratory careers first learned about these opportunities.

The American Society for Clinical Pathology (ASCP) collaborated with the University of Washington Center for Health Workforce Studies on a groundbreaking study that looks at how people came to their careers in the laboratory. This study, "Career pathways into the medical laboratory workforce: Education, exposures, and motivations," sheds light on how individuals enter the laboratory field, what draws them in, and what obstacles they face.

For those already in their careers, understanding this journey is not just a matter of curiosity; it's a leadership imperative. We must collectively reevaluate how we engage with the future of our workforce. This study provides a data-driven roadmap to doing just that, and I encourage you to watch the short video on The Pathologist website to learn more about what the study reveals.

Many of those surveyed reported that they only learned about pathology and laboratory medicine through a relative, a college counselor, or a chance elective class. If we want to build a workforce that is prepared to meet the healthcare challenges of today and tomorrow, we need to make the path into this profession more visible, accessible, and intentional.

This is where we can make a tangible difference, being in the unique position to mentor students, support outreach initiatives, and partner with high schools, community colleges, and universities to broaden access. By sharing our stories, offering shadowing opportunities, or participating in community events, we help demystify the profession and inspire the next generation.

The ASCP–University of Washington study is more than just an academic analysis – it's a call to action. It provides the healthcare community with a blueprint for change. But change doesn't happen in a vacuum. It requires every stakeholder in laboratory medicine to take responsibility for the future of the profession. The question we should all be asking is: what are we doing to ensure the next generation of laboratory professionals can find their way in – and thrive?

"If we want to build a workforce that is prepared to meet the healthcare challenges of today and tomorrow, we need to make the path into this profession more visible, accessible, and intentional."

The journey into laboratory medicine should not be accidental. It should be intentional, inclusive, and supported every step of the way. Let's rise to meet that challenge together.

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Meet Methylation Man!

In conversation with Matija Snuderl, the pathologist behind the brain cancer diagnostic superhero

"Not all heroes wear capes. Some wear coats – lab coats." With these words, Methylation Man embarked on a series of epic diagnostic quests in The Pathologist in 2024, cracking brain tumor classification conundrums with the power of DNA methylation profiling.

As with any great comic strip, naturally we are curious about the man behind the superhero. We caught up with Matija Snuderl, MD, Director of Molecular Pathology at NYU Langone Health, to learn more about the tools in Methylation Man's utility belt.

What inspired the creation of Methylation Man?

Brain tumors are among the most malignant tumors in the human body. Many of our patients are children with brain cancer, and we often find ourselves in the position of delivering the most difficult news to patients and parents.

Because DNA methylation profiling helps oncologists refine the diagnoses of brain tumors, it can help patients greatly; but it's also a bit of an enigma. If I tell my patients that I'm going to examine the methylation profile of their DNA, they don't know what that means. The same goes for many neurosurgeons and oncologists, who might have learned about the concept in medical school and not thought about it since.

So, we are often in the situation of explaining a complex concept over and over and trying to find the right language. I started to think about the best way to explain what we do. I've given a lot of educational and scientific talks, but I felt that a different approach was needed.

I'm based in New York, which, as we know, is where all the superheroes come from. I came up with the idea that DNA methylation profiling needed its own superhero to champion the technique, explain it simply, and show how it helps doctors to solve diagnostic conundrums.

What is the aim of the comic strips?

One of the aims is to provide easily digestible information on a complex condition for patients and their families. Few of them have any concept of the intricacies of tumor diagnostics, and often find the medical lingo used in discussions of blood tests, imaging, and molecular testing overwhelming.

But the testing is really critical because it defines their disease management, so we wanted the comic strips to help explain what's involved, and how it helps us establish the best care.

The other aim is to help raise awareness of brain tumors. Because they are uncommon, there is little awareness of how difficult they are to treat. We wanted to give our patient advocates and fundraising partners a tool to help them easily explain the important diagnostic work that we do.

What is the role of DNA methylation profiling in advancing tumor classification?

DNA methylation can be regarded as a fingerprint of a cancer cell that contains information on where the cell came from it and how it became cancerous.

While all our cells contain the same genes, they all serve different functions in the body: tissue, organs, bones, and so on. So what makes brain cells look and function in a different way to, say, heart cells?

Well, DNA methylation – a type of epigenetic modification – shuts down some parts of the genome that the particular cell doesn't need. All the cells have the same DNA code, but with different epigenetic modifications that determine their function.

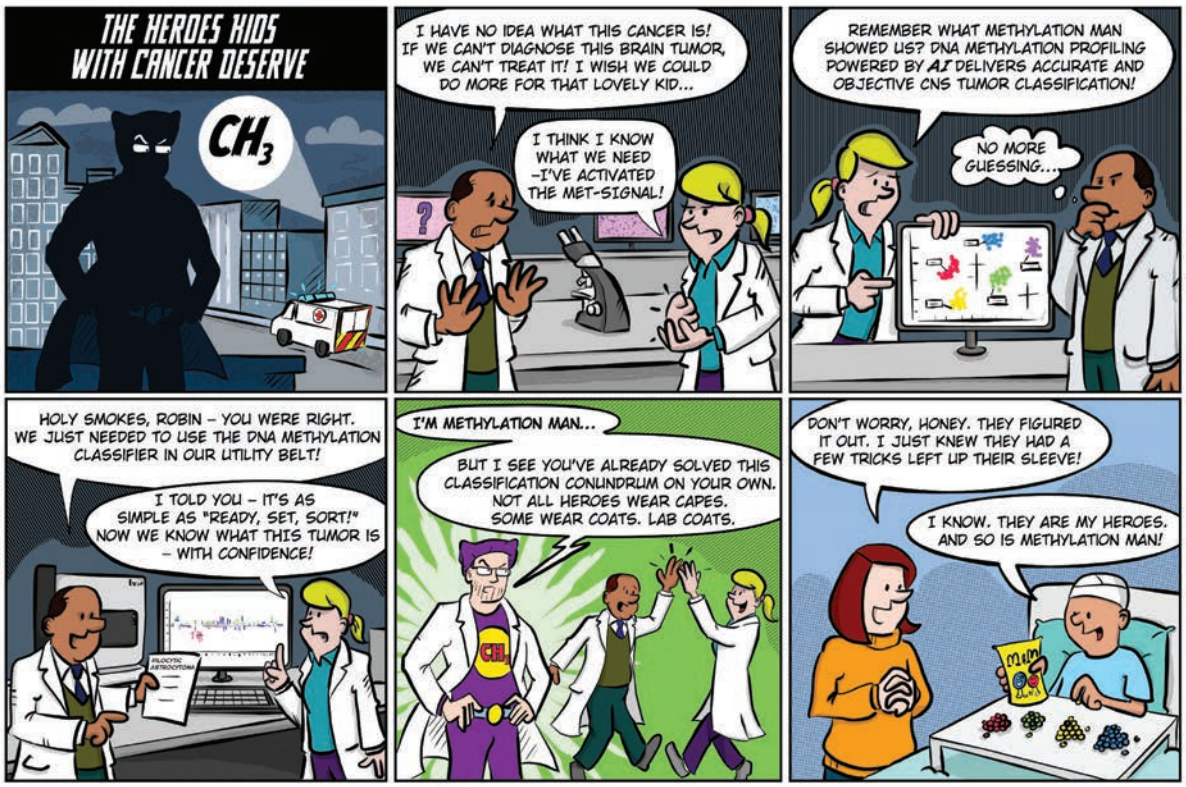
This epigenetic fingerprint tells us about a cancer cell's origins and the specific DNA mutations that are driving the tumor growth. That is really useful for the classification of cancers.

How are technologies such as next-generation sequencing and AI analytics driving expansion of DNA methylation applications?

The most common method of analyzing DNA methylation is using methylation arrays. Imagine a tiny tray of microscopic beads, each with a fragment of DNA from a tumor attached. Each fragment shows a different color signal according to whether it binds to the methylated or unmethylated tag. A sensitive camera then reads the color signal for every position in the human genome, from which a map of the methylation patterns can be determined.

Next-generation sequencing is also used for DNA methylation profiling. And new technologies are on the horizon, which will allow even greater sophistication.

"I started to think about the best way to explain what we do. I've given a lot of educational and scientific talks, but I felt that a different approach was needed."



Now let's consider how we analyze the information. Methylation arrays might compare more than 900,000 sites across the genome, which generates a huge amount of data. We use a variety of computational approaches – best described as machine learning or AI – to process the data.

For every class of a tumor, we try to identify a distinct DNA methylation signature. We then use that signature to train our machine learning algorithm to identify each tumor type from its epigenetic fingerprint. After testing the algorithm, we develop a workflow through which it can analyze and classify unknown tumors for our patients.

AI-enabled DNA methylation tumor classification, along with next-generation sequencing, is now expanding applications beyond the central nervous system. Some examples are sarcomas, hematological malignancies, and kidney tumors.

What is being done to improve patient access to DNA methylation profiling?

We want to avoid the situation where DNA methylation profiling is only available to patients who are able to travel to a specialist cancer center. My goal has always been to make this technique accessible as a regular laboratory assay that can be set up anywhere and reimbursed by insurance. This was important, because we can't afford to limit applications to the handful of sites that have access to philanthropic funding.

My team has spent a lot of time developing protocols that can be deployed in any lab with the relevant technology. We also share validation protocols so other teams don't have to reinvent the wheel, enabling a "plug and play" approach on both the laboratory and computational side.

Of course, the data interpretation does require specialist knowledge of both the disease and the DNA methylation signatures. However, AI speeds up this process and opens up a test that is incredibly powerful in the hands of an experienced pathologist who can interpret the results in context. I always say that AI will not replace pathologists or physicians, but those who use AI will replace those who do not use it.

What's next for Methylation Man? What are some of the problems he still needs to solve?

There's still so much more we need to discover with DNA methylation. There's a hint in a couple of episodes of the comic that DNA methylation is applicable to more than just brain tumors. There are other cancers that will really strongly benefit from DNA methylation classification.

My other dream is discovering how we can translate DNA methylation signatures into therapeutic discovery. We spent 10 years trying to better classify tumors for diagnosis and showed we can avoid more than 15 percent of misdiagnosis and diagnostic errors using DNA methylation. My hope is that, in the next 10 years, we can analyze this trove of data we collected and really focus on finding new therapeutic targets.

Perhaps one day Methylation Man will not only predict what's going to happen with a patient, but perhaps change the outcome with a better therapy.

And, of course, after comic strips there is always a movie, right?

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Diagnosing the *Disconnect*

Exploring the double burden of diagnostic inaccessibility and brain drain in global healthcare

Low- and middle-income countries (LMICs) face a series of challenges in providing diagnostic services and patient care. With trained professionals leaving to progress their careers in high-income countries, and increasing costs dwindling resources, those left behind are treading water. Here, we hear from three experts hoping to make a difference. Augustine Onwunduba and Yoel Lubell talk about the introduction of low-cost biomarker testing in LMICs; and Sipho Kenneth Dlamini discusses why the concept of "brain drain" might be worsening the workforce decline.

Respiratory Disease: From Scarcity to Solutions

How low-resource-focused innovations in biomarker diagnostics are shaping the future of global health

Despite advances in technology and medicine, half the world's population has no access to essential diagnostics (1). For individuals living in LMICs, this diagnostic gap can be life threatening.

But not all hope is lost. Researchers are exploring ways to introduce low-cost biomarker testing into low-resource settings. Here, we turn to two experts exploring the possibilities in the respiratory infections landscape.

What gaps exist in current diagnostic strategies for respiratory infections in LMICs, and how do these gaps affect patient care?

Augustine Onwunduba: Because rapid diagnostic tools are often unavailable in low-resource areas, primary care providers usually treat suspected respiratory infections based on symptoms alone (2). As a result, they often prescribe antibiotics without confirming the cause. However, most respiratory infections don't need antibiotics (3), so this approach can lead to unnecessary use. This, in turn, contributes to the spread of antimicrobial resistance (AMR) (4), a problem discussed later in this article.

Yoel Lubell: Agreed, and this issue is made worse by limited access to follow-up care or the ability to escalate treatment if a patient gets worse. As a result, antibiotics are overprescribed, driving AMR and possibly leading to patients receiving the wrong kind of care.

A key issue is that diagnostic strategies don't always match public health goals. Some focus too little on reducing unnecessary antibiotic use, while others may be too strict, risking the denial of needed treatment.

When developing new diagnostic tools – especially those based on biomarkers – it's often unclear what the main goal is. Are we trying to tell bacterial and viral infections apart to guide antibiotic use? Or are we trying to spot patients who are likely to get worse, regardless of the cause? Without clear goals, even good diagnostics might not improve patient care or support public health efforts.

What are the biggest challenges to implementing biomarker-based diagnostics in low-resource settings?

AO: There are two key challenges. Firstly, most patients pay for healthcare themselves, so they may not want to spend money on a test. And secondly, community pharmacies – where many respiratory infections are treated – are private businesses that make money from selling antibiotics, so they may be reluctant to offer testing. Any plan to introduce testing must take these issues into account.

YL: Other barriers are cost, weak supply chains, lack of training, and limited infrastructure. Even basic tests like lateral flow tests are hard to implement if they seem expensive compared to the treatment they guide, making them appear less useful. Health workers also need training – not just on how to use the tests, but on how to understand the results, adjust treatment decisions, and clearly explain the results to patients. This can be especially difficult in busy, under-resourced clinics.

What are the key criteria for selecting biomarkers for use in diagnostics in environments with limited resources?

YL: In low-resource settings, a good biomarker must be:

- Stable and easy to understand without lab equipment
- Affordable
- Simple to use with little training
- Helpful for guiding antibiotic decisions
- Usable with a finger-prick blood sample in a rapid test format

There are already many low-cost C-reactive protein (CRP) point-of-care (POC) tests available that meet these needs, especially for assessing respiratory infections. While new tests are being developed, there's a strong case for using proven biomarkers and technologies that are already well studied and understood.

AO: Affordability is arguably the main factor – biomarker tests must be affordable for patients or whoever is paying for them. That's why CRP is a good option in these settings: low-cost CRP test kits, like semi-quantitative lateral flow tests, are already available.

How do you ensure the sensitivity and specificity of biomarker-based tests when used outside highly controlled laboratory environments?

YL: You don't – at least, not at the same levels of accuracy that you'd find in a well-equipped lab in a high-income setting. Instead, you trade a bit of accuracy for practicality. For example, lateral flow CRP tests aren't as precise as lab tests, but they're still accurate enough to guide treatment – especially with cut-offs like 10-40 mg/L, which help distinguish viral from bacterial infections. Our real-world studies in Vietnam, Thailand, and Myanmar show these tests work well, even in tough field conditions.

Meet the Panelists

Augustine Onwunduba is Lecturer in Clinical Pharmacy and Pharmacy Management, Nnamdi Azikiwe University, Awka, Nigeria.

Yoel Lubell is Professor of Global Health at the University of Oxford, UK, and head of the Economics and Implementation Research Group in the Mahidol Oxford Tropical Medicine Research Unit (MORU) in Bangkok, Thailand.

AO: As Yoel says, CRP tests aren't perfectly accurate – they don't always detect every case or rule out others. That's why clinical judgment and other test results should be used alongside CRP results when deciding whether to give antibiotics. For example, if a patient has a high CRP level, a malaria test might help confirm if malaria is the cause, which could reduce the need for antibiotics. On the other hand, clinical judgement alone could inform antibiotic use, despite normal or low CRP.

Why is there a low CRP uptake in LMICs – what are the benefits and limitations of these tests?

AO: CRP testing helps improve responsible antibiotic use for suspected respiratory infections in both public and private primary care in low-resource settings – and it's cost-effective. However, its accuracy isn't perfect.

In our trial in Nigeria (5), CRP tests were used in only 21.4 percent of the visits where we expected them. There were a few reasons for this low uptake. Some patients refused the test because they worried they couldn't afford both the test and antibiotics if needed. Also, some pharmacy staff, lacking a clear understanding that most respiratory infections don't need antibiotics, began to distrust the test kits when results often pointed away from antibiotic use. To improve uptake, we recommend making the test more affordable and training pharmacy staff more thoroughly.

YL: CRP testing is still used infrequently, and the reasons vary by setting. Some common challenges include the fact that it disrupts long-standing habits and adds complexity to already busy clinical routines. Also, avoiding antibiotics – even when appropriate – may not seem important to healthcare workers or patients, especially when there's pressure to give treatment quickly.

While it's helpful to highlight how overusing antibiotics contributes to drug resistance on a population level, it's just as important to explain the personal risks – like side effects, harm to the gut microbiome, and longer-term health issues from unnecessary antibiotic use.

Local factors also affect uptake. In a recent trial in Vietnam (6), even with strong support for CRP testing, few patients received the test because family members often collected treatment instead. Still, when the test was used, it significantly reduced antibiotic use without harming patients.

CRP tests, like all biomarker tools, have some drawbacks. Inflammation from non-bacterial causes can lead to false positives, and some early or unusual bacterial infections may not be detected. But overall, CRP testing improves how antibiotics are used – especially in places where overprescribing is common. Making CRP testing routine with today's tools can also help us learn more and prepare for the rollout of new diagnostic tests in the future.

Can you briefly discuss your study and how CRP testing affected results compared to standard processes?

AO: In Nigeria, community pharmacies give antibiotics to 81 percent of patients with suspected respiratory infections – often without a prescription or diagnosis. In our trial, when we gave these pharmacies CRP test kits and trained them to use the tests to guide antibiotic use, the chances of them giving antibiotics without a prescription dropped by 72 percent.

YL: In our large trial in Vietnam, we aimed to test CRP use in real-world conditions. To keep things realistic, we didn't place research staff at the clinics, and ethics committees allowed us to skip individual patient consent because the test was already well studied. This helped avoid disrupting routine care and showed how the intervention might work in everyday practice.

However, the study took place during the COVID-19 pandemic, when many people avoided visiting clinics. This likely limited how many patients were reached and reduced the full impact of the intervention.

Still, the results were encouraging. Antibiotic use dropped from 98 percent to 93 percent overall, and to 71 percent among patients who actually received a CRP test. There were no negative effects on patient health or recovery. But the low use of testing shows that simply offering a new tool isn't enough. To create lasting change, broader support is needed – such as staff training, better integration into clinic routines, and incentives to encourage appropriate antibiotic use.

How does CRP fit into symptom agnostic screening?

YL: CRP isn't truly symptom-agnostic – it performs best when a bacterial infection is suspected, helping to rule out the need for antibiotics. Still, in cases where the cause of illness isn't clear, CRP provides a practical way to assess risk and guide more targeted treatment. It's especially helpful when symptoms alone don't give enough information to make a clear decision.

If not CRP, are there any other POC tests that can support infectious disease diagnostics in LMICs?

YL: New multiplex biomarker tests are being developed to improve how respiratory and febrile illnesses are managed in LMICs. Many of these tests still include CRP, combined with one or two other markers to improve accuracy – since CRP alone has limitations.

However, this improved accuracy comes at a higher cost. These newer tests are more expensive, and it's hard to judge whether the extra precision is worth the price, especially since current economic models don't always factor in the long-term savings from avoiding AMR.

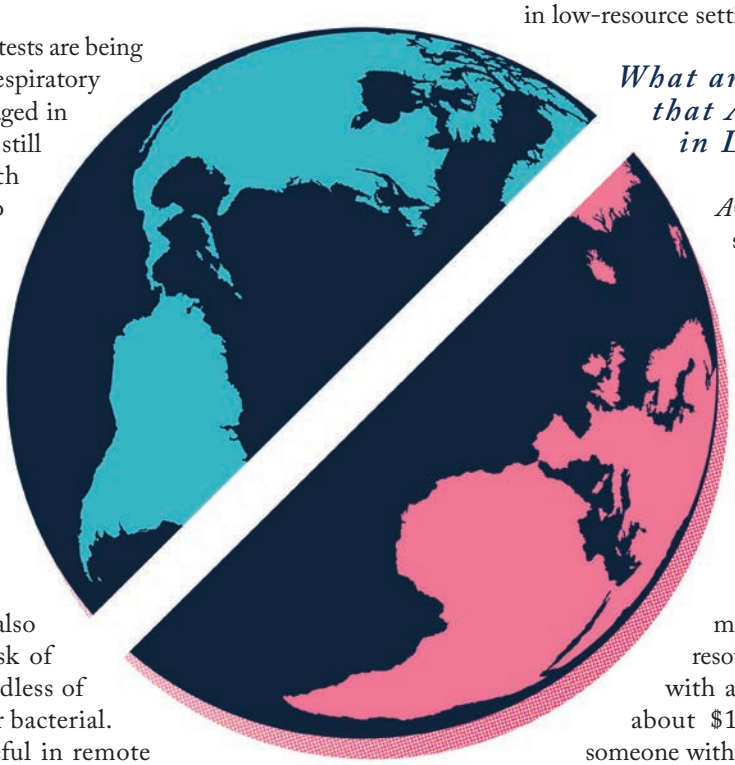
Some of these tests may also help identify patients at risk of becoming seriously ill, regardless of whether the illness is viral or bacterial. This could be especially useful in remote areas by helping decide when a patient needs to be referred to a higher-level facility. CRP alone isn't ideal for this purpose. Other markers, like sTREM-1 and ANG-2, may be better at predicting severe illness. We're currently working with industry partners to develop POC tests for these markers, to give frontline healthcare workers better tools in low-resource settings.

Do you believe POC testing will play a big part in diagnostics in LMICs moving forward?

AO: Absolutely – relevant stakeholders in low-resource settings are encouraged to consider implementing CRP testing intervention for suspected respiratory infection in primary care.

YL: The pandemic showed that large-scale testing for respiratory illnesses is possible – not just in hospitals, but even in communities. Along with the long-standing success of malaria rapid tests in remote areas, this proves that POC testing can work well in LMICs.

Looking ahead, POC testing will likely become even more important. New technologies – like advanced tests that measure both host biomarkers and specific pathogens – are being developed. When paired with mobile apps, electronic decision tools, and AI, these innovations could help fill gaps in lab services and make up for the shortage of highly trained health workers in low-resource settings.



What are the challenges that AMR presents in LMICs?

AO: AMR occurs when bacteria stop responding to antibiotics that once worked. It's a serious health problem, especially in low-resource settings. In 2019, the death rate from bacterial AMR was higher in Sub-Saharan Africa (23.7 deaths per 100,000 people) than in high-income countries (13.0 per 100,000) (7).

AMR also makes infections more expensive to treat. In low-resource settings, treating someone with a resistant infection can cost about $12,442 more than treating someone with a non-resistant infection (8).

YL: We're just beginning to understand all the complex factors that drive AMR – and many go beyond antibiotic use in healthcare. Things like farming practices, climate change, conflict, poverty, and inequality all play a part, especially in LMICs. At the same time, many people in these settings still don't have enough access to the antibiotics they truly need. So, any plan to fight AMR must carefully balance reducing misuse without limiting access to life-saving treatment.

That said, overuse of antibiotics in human health – especially in clinics and communities without proper diagnostic tools – is a major and avoidable cause of AMR. In LMICs, this is clear when it comes to treating respiratory illnesses, where antibiotics are often given without a confirmed need or bought over the

counter without regulation. While it's important to look at the bigger picture of AMR, cutting unnecessary antibiotic use in primary care – especially for respiratory infections – is one of the quickest and most achievable steps we can take. Widening access to affordable, effective diagnostic tests is key to making that happen.

Are there ongoing trials or pilot programs that are testing new biomarker-based diagnostic tools in the field?

YL: We recently ran a trial in Cambodia (9) that combined CRP testing and pulse oximetry with an electronic decision support system to help manage acute fever cases. While final data is still being analyzed, we've already gathered feedback through focus groups and interviews with healthcare workers and policymakers. Overall, the response has been positive. People saw the value of these tools in helping make better clinical decisions, especially where lab resources are limited.

However, one key takeaway was clear: for these tools to work well, they must be co-developed with the people who will use them. Involving frontline workers in the design process is essential to make sure the tools are practical, user-friendly, and likely to be adopted long-term.

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Global Health, Local Losses

Brain drain isn't just a workforce issue – it's straining diagnostics, stewardship, and survival in low-resource settings

The emigration of highly trained and qualified people from their home country – also known as "brain drain" – continues to negatively impact diagnostics in LMICs. Alongside already pressing concerns of limited access to essential services, laboratory professionals in LMICs are struggling to manage increasing caseloads.

Here, we speak with Sipho Kenneth Dlamini, Associate Professor of Infectious Diseases at the University of Cape Town, South Africa, about the importance of tackling brain drain before it's too late.

How would you describe the current landscape of diagnostic capacity in LMICs?

Diagnostic capacity in LMICs is currently too limited to meet the health needs of their populations. Access to testing is poor, and diagnostic systems are often underfunded and unsupported. As a result, infrastructure is weak, leading to serious gaps in healthcare. This contributes to health inequalities both within and between countries. The COVID-19 pandemic made these problems even more visible from a diagnostic point of view.

How does the limited number of trained pathologists in LMICs affect core diagnostic services?

Shortages of trained healthcare workers leads to delays in diagnosis and treatment, which harms patient care and health outcomes. For example, limited diagnostic capacity makes it harder to effectively treat diseases like tuberculosis. It also weakens antimicrobial stewardship programs, which rely on diagnostics to fight AMR. Other conditions affected include HIV, malaria, cancer, and chronic illnesses like heart and kidney disease.

Many programs aim to train pathologists and laboratory professionals in LMICs. In your view, how successful have these efforts been in retaining talent locally?

According to published reports and the 2023 World Health Assembly (1), many countries have committed to improving diagnostic capacity. However, progress has been slow and varies by country due to different challenges. Some nations have made strides by creating national strategies, updating regulations, and adopting new technologies. Still, access and affordability remain major issues in LMICs.

These efforts can help retain skilled professionals, but the reasons people leave their countries are complex. A safe and supportive work environment is important, but so are broader social factors – such as quality of life and political stability – which are often key reasons for migration.

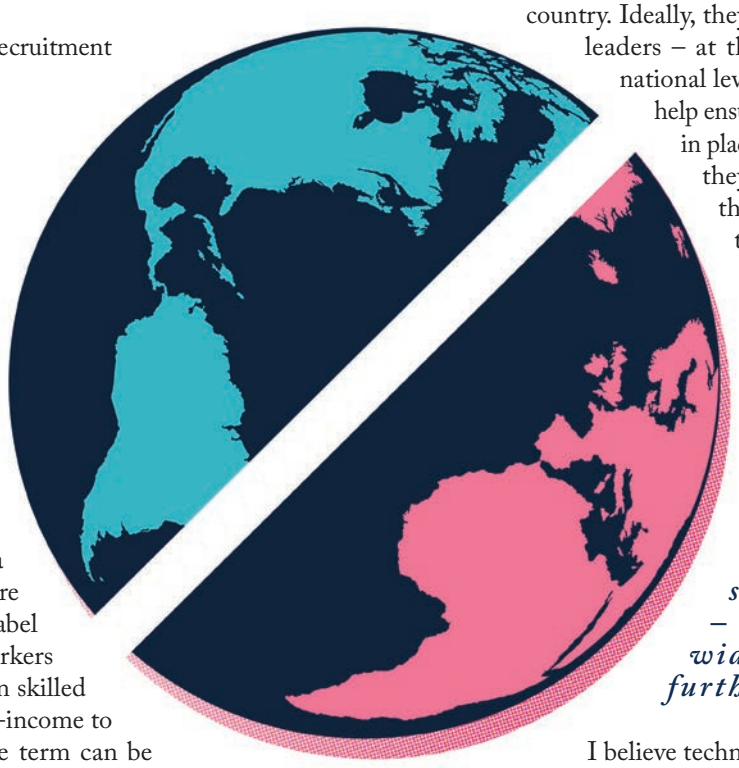
What are the primary drivers of brain drain in pathology and lab medicine?

Several key factors drive challenges in pathology and laboratory medicine:

- **Economic:** low pay, unstable economies, and limited job opportunities
- **Professional:** outdated infrastructure, lack of research support, burnout, and poor leadership
- **Social:** desire for better living conditions, social unrest, and lack of professional recognition
- **Workplace:** unsafe environments, harassment, and fear of malpractice
- **External pressures:** active recruitment from other countries and better training or career opportunities abroad

At ESCMID Global 2025, you suggested the term "brain drain" is unhelpful – could you expand on this?

I believe we need to rethink the term brain drain because it carries a negative message. It suggests that only the most talented people leave a country, while those who stay are somehow less capable. This label isn't used when unskilled workers migrate, nor is it applied when skilled professionals move from high-income to low-income countries. So the term can be misleading and unfair.



To what extent does international collaboration – such as fellowships or exchange programs – help to alleviate brain drain?

International partnerships that aim to improve training and reduce brain drain are helpful but often have limited impact. They can't solve deeper problems like weak healthcare funding, economic instability, or inflation. There are also not enough training spots or fellowships to meet the demand.

For these programs to succeed, all stakeholders need to work together. Too often, exchanges or fellowships happen in isolation and focus only on the individual – not on the system they'll return to. As a result, many professionals gain valuable skills abroad but can't apply them at home due to poor infrastructure and lack of support.

What advice would you give to a young pathologist from an LMIC who is eager to pursue advanced training abroad but also wants to give back to their home country?

It's important to encourage young people to pursue advanced training abroad, especially if it's not available in their home country. Ideally, they should talk to local health leaders – at the institutional, district, or national level – before they go. This can help ensure there's some infrastructure in place to support their skills when they return. Planning ahead in this way makes it more likely that their training will lead to lasting, meaningful improvements in healthcare for their country.

Do you think digital pathology, AI, and remote diagnostics could help address some of the workforce shortages in LMICs – or do they risk widening the gap further?

I believe technology is valuable and should be embraced – it's a key tool that can help meet health needs in LMICs, especially where there are shortages of healthcare workers.

In your opinion, what would a sustainable, context-sensitive solution to diagnostic workforce development in LMICs look like?

In my ESCMID Global talk, my main message was to highlight that the global health workforce should be seen as a shared resource. Everyone benefits when healthcare workers are distributed more fairly around the world. Training and developing healthcare workers shouldn't be the responsibility

of individual countries alone. Instead, we should explore global training models that support workforce sharing across borders.

My concern is that if we stick with the current system, LMICs will continue to fall behind. They often lack the resources to train or keep highly skilled workers and can't compete with wealthier countries. Sometimes, high-income countries find it cheaper to recruit workers from poorer countries rather than invest in training locally. This can lead to serious shortages in the countries that are losing workers.

That said, LMICs also have an important role to play. They need to follow through on the commitments they've made – especially those focused on expanding access to diagnostics and developing the health workforce. This includes improving working conditions, investing in diagnostic infrastructure, and making sure diagnostic services are well integrated into health systems. Regional and cross-country collaborations to build diagnostic capacity are already happening, and these efforts should be supported and expanded.

"Training and developing healthcare workers shouldn't be the responsibility of individual countries alone. Instead, we should explore global training models that support workforce sharing across borders."

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MOLECULAR PATHOLOGY

Better Biomarker Testing

Canadian study highlights gaps in molecular diagnostics for lung cancer and recommends best practice

With lung cancer continuing to be the leading cause of cancer mortality in Canada and many other countries, and precision medicine taking over every stage of treatment, the stakes for timely and accurate molecular diagnostics are more important than ever.

A new study – conducted through the Canadian Pathology Quality Assurance – Assurance qualité canadienne en pathologie (CPQA-AQCP) End-to-End Quality Assurance (EQA) program – identifies critical differences in diagnostic turnaround times and testing quality.

We connected with Brandon Sheffield, Molecular Pathologist in the Division of Advanced Diagnostics at the William Osler Health System (Osler) and lead of the EQA program of the CPQA-AQCP, to find out what the study revealed, and its implications for biomarker testing quality.

What inspired this study?

Lung cancer is the number one leading cause of cancer-related mortality in Canada. Most patients seek care when they already have metastatic disease (stage IV), are very sick, and at risk of death. Frustratingly, many oncologists in Canada are unable to offer state-of-the-art treatments because they don't receive biomarker test results in a timely manner – an issue that remains largely unrecognized by most laboratories.

Quality is a cornerstone of laboratory practice. Biomarker testing for lung cancer and other solid tumors is commonly performed using next-generation sequencing (NGS) or immunohistochemistry (IHC). While external quality assurance programs generally only assess the accuracy of results, they have rarely evaluated turnaround time, which is a critical factor in timely patient care, especially for lung cancer.

We set out to develop a biomarker quality assurance program that was more suited to the current landscape of precision medicine, one that incorporates turnaround time and integrates medical oncologists' decision-making as a key component of the process.

Who was involved?

The study was put together by the Canadian Pathology Quality Assurance (CPQA), which has been providing external quality assurance for IHC testing in Canada for decades.

All Canadian lung cancer testing laboratories were invited to participate, and 13 opted in to the exercise.

What did the findings reveal?

Laboratories, for the most part, were able to provide accurate biomarker results. But even though many labs arrived at the same result, the turnaround time ranged anywhere from 5 to 57 days. Surprisingly, only two labs were able to report results within two weeks of receiving the test samples and meet national and international guidelines. Three labs had turnaround times exceeding a month, which was considered unacceptable.

Even though many labs provided the correct test results, the long delay in providing those results led oncologists to make suboptimal treatment decisions for the fictional patients in the exercise.

Essentially, the study found that many lung cancer patients in Canada might receive suboptimal treatment due to delays in receiving their biomarker test results.

What implications could this research have on biomarker testing quality?

Three labs within the study were found to have an "optimal" performance. Interestingly, these labs all utilized different methodologies to achieve their biomarker results. What each of these labs had in common was the use of integrated reports – or a single biomarker report for both NGS and IHC, signed by a single pathologist.

This feature was felt to be indicative of a simpler and more straightforward workflow that facilitated fast and efficient results. This also highlights the need for molecular pathologists to be involved and work with multiple modalities.

This study highlights significant disparities in lung cancer testing and treatment, and highlights the need for ongoing EQA participation by laboratories. The CPQA has now conducted three of these exercises and observed that laboratories participating consistently tend to improve their turnaround times.

INFECTIOUS DISEASE

Interleukin-6 in the Fight Against Sepsis

Biomarker shows diagnostic potential in a real-world setting

Sepsis remains a leading global cause of mortality, accounting for around 11 million deaths annually. In an attempt to improve detection of this life-threatening condition, a team of researchers in Dublin, Ireland, tested the biomarker performance of Interleukin-6 (IL-6). We connected with Sean Whelan, lead author of this study, to learn more about the findings.

What motivated you to focus on sepsis in neonates, children, and pregnant women specifically?

Diagnosing sepsis accurately and quickly in these groups is challenging. In neonates, confirmed sepsis is rare, so we often rely on clinical signs and biomarkers to guide treatment – but these tools aren't always reliable. In children and pregnant women, many conditions can look like sepsis. For example, bleeding, eclampsia, or even labor in pregnancy can mimic sepsis symptoms, making diagnosis difficult. That's why having reliable sepsis biomarkers for these populations is so important.

How does the study build on existing research on IL-6 as a biomarker?

Other studies have used IL-6 as a sepsis biomarker, which encouraged us to adopt it in our practice. What makes our study unique is that it looks at how IL-6 performs in everyday clinical settings, not just in controlled trials, and across three different patient groups.

How did IL-6 perform as a biomarker across the different patient groups?

Overall, IL-6 outperformed the other biomarkers we tested – CRP, PCT, and the neutrophil-lymphocyte ratio (NLR) – in all groups and for both diagnostic categories: physiological status and infection cause.

There were two exceptions, however, where IL-6 did not show a statistically significant advantage:

- In pregnant women for assessing physiological status (normal, SIRS, sepsis, or septic shock), IL-6 and NLR performed similarly (area under the receiver operating characteristic curve [AUROC]: IL-6 = 0.78, NLR = 0.72).
- In newborns, IL-6 and PCT also showed similar performance (AUROC: IL-6 = 0.86, PCT = 0.74).

How does this biomarker perform in differentiating between bacterial and viral infections?

We evaluated IL-6 in both pediatric and maternal patients. In children, IL-6 was highly effective at distinguishing bacterial from non-bacterial infections (including viral and no infection), with a sensitivity of 86 percent and specificity of 82 percent – better than CRP (77 percent sensitivity) and PCT (55 percent). The AUROC was 0.91, indicating excellent diagnostic accuracy.

In pregnant women, IL-6 also performed very well, with an AUROC of 0.94, sensitivity of 88 percent, and specificity of 91 percent. In contrast, CRP and PCT were much less reliable in this group – CRP had only 33 percent sensitivity, and PCT had 50 percent specificity.

It's important to note that these results apply to patients already suspected of having sepsis. Although distinguishing bacterial from viral causes is also crucial in a broader population, that was not the focus of this study.

Can this test be utilized in other areas, such as low-resource or point-of-care settings?

We measured IL-6 using an electrochemiluminescence immunoassay, which runs on equipment already found in many medical labs. This makes adoption easier and allows for quick results. However, using this technology in low-resource settings is more difficult. Some studies have explored IL-6 test strips with optical readers as an alternative, but more research is needed before they can be used reliably in clinical practice.

Are there any pre-analytical or sample handling considerations that pathologists and lab staff should be aware of?

No, the testing was done by our clinical biochemistry team, including Professor Elsammak, a co-author and Consultant Chemical Pathologist. They were pleased with how well the assay performed. We've also extended testing hours to ensure results reach clinicians quickly, helping them care for these critically ill patients.

What's next for this research?

We now use this biomarker regularly in our clinical practice, and it's included in our hospital's guidelines for managing suspected sepsis. Over time, more clinicians have started using it as they've seen its value, and test requests have increased.

From a research standpoint, we'd ideally like to see a prospective study to measure how IL-6 impacts patient outcomes and whether it's cost-effective – but such a study would be a large effort, and as far as we know, none is currently planned.

Any expectations or hopes for the future of sepsis diagnosis?

My main hope is that pathologists can keep working closely with clinicians to improve early sepsis detection – especially in pregnant women and children, who are often underrepresented in research.

This study was presented at ESCMID Global 2025.

DIGITAL PATHOLOGY

Compatible (Digital) Partners

Why DICOM compliance is essential for digital imaging in pathology and beyond

Alan Byrne is Director of Global Marketing for Pathology at Agilent and serves on the Board of Directors of the Digital Pathology Association. His experience working both for manufacturers and in frontline lab management gives him a unique perspective into diagnostics and the technology that drives it.

Taking full advantage of his insights, we picked Byrne's brains on the importance of digital imaging and communications in medicine (DICOM) in enhancing interoperability, affordability, and sustainability in digital pathology.

What is your professional background?

I'm a scientist by training, with higher qualifications in both precision medicine and business administration. I actually started my career as a salesperson, progressing to local product management and general management positions within the pharma and in vitro diagnostics sectors in Ireland and further afield.

During that period, I became very interested in clinical laboratory management and, in particular, the interface between testing and treatment, and I took a role at Beaumont Hospital, Dublin, as a business manager for the Directorate of Laboratory Medicine.

My role was essentially to work at the interface of the clinical and scientific leadership teams and the hospital group's C-suite teams. I ensured that the lab was adequately resourced to achieve the correct mix and volume of testing in accordance with quality, cost, revenue generation, and modernization targets.

Being equipped with both industry and in-lab experience allows me to see both sides of the coin and, I can tell you, the customer's needs always come first for me. This experience and mindset led me to Agilent and, in particular, to the pathology division. Now, as a director of product marketing, I have responsibility for two areas: pricing and analytics, and digital pathology. I've been in the role here for a little over three years.

How does DICOM compatibility enhance the integration of digital pathology data with other imaging modalities in a clinical diagnostics workflow?

It provides a standardized framework for managing and sharing images across modalities such as computed tomography, X-ray, magnetic resonance imaging, and now digital pathology too. Simply put, it allows images to be shared across different systems and devices, regardless of the manufacturer. Essentially, DICOM is a standard.

Here is a real-world example of DICOM in action: imagine a pathology laboratory that has, over the years, installed whole slide imaging (WSI) scanners from several different manufacturers. Now imagine each scanner had DICOM compatibility – this would mean that they could all work together with an image management system (IMS). This interoperability enhances efficiency, accuracy, and comprehensive diagnostics, and also, in an ideal world, allows labs to utilize existing onsite technology.

Another key point is that DICOM also allows the integration of WSI scanners with other technologies – namely picture archiving and communication systems (PACS) and Vendor Neutral Archives (VNAs). This allows pathologists to share images with colleagues in other departments, such as radiology, to better facilitate multidisciplinary team meetings and tumor boards. This integration points to enhanced efficiencies, accuracy, and more comprehensive diagnostics.

What challenges do laboratories face when implementing DICOM standards in digital pathology, and how can these be addressed to improve interoperability?

One challenge is around product selection and procurement. Some instrument and software manufacturers may offer DICOM functionality as an add on, rather than an off-the-shelf offering. Some may claim that their technology is DICOM compatible, but interoperability may not yet be proven.

This is where organizations like the Digital Pathology Association are supporting the community. They organize "connectathons" to challenge the compatibility of different systems. Having said that, I think we are moving towards a situation where DICOM becomes a sort of lowest common denominator for digital pathology systems – if suppliers don't have it, they won't be in the game.

Another obstacle is the preparation for the actual integration at the institution. There is little point proceeding with

procurement until existing systems have been fully evaluated. This may include evaluation of the hospital information system itself, as well as the laboratory information system, to understand their capabilities and compatibility with DICOM. Whilst interoperability is the way forward, the institution may not be ready for it, since not all PACS or VNAs in use today can accommodate the file sizes and intricacies of whole slide imaging, but that's another conversation.

With the increasing adoption of AI tools in pathology, how does DICOM compatibility facilitate the use of machine learning algorithms and decision support systems?

Digital pathology generates huge amounts of image data and metadata. DICOM's standardized approach simplifies the storage, retrieval, and management of these images, making it more efficient to ingest the datasets required for training machine learning models.

Looking to the future, I feel that this standardization will increase user confidence and adoption of AI tools for digital pathology.

Another consideration here is the increasing importance of digital pathology within companion diagnostics. As an example, there are therapies under development that are using digital tools as part of the biomarker discovery process and beyond. I believe it is realistic to expect that we will soon see companion diagnostic assays used in conjunction with digital decision support algorithms in the clinic. I say this because some of these emerging therapies (antibody-drug conjugates as an example) may require very complex pathological interpretation. In these cases, the use case for DICOM standardized AI-driven image analysis is compelling.

Given the massive file sizes associated with whole slide imaging, what are the critical factors laboratories should consider when selecting data storage solutions?

This is a very common question. For me there are a few key factors. First, it depends on how many slides the lab processes per year and how many it plans to digitize now and into the future. Data storage is important for all, but it is a major concern for high-throughput digital labs, or those that process a lot of immunohistochemistry, owing to increased file sizes.

"I think we are moving towards a situation where DICOM becomes a sort of lowest common denominator for digital pathology systems – if they don't have it, they won't be in the game."

Second, we need to consider the local set-up. The institution may have an existing on-premise or cloud-based system available, particularly if they have a modern radiology unit, or a new system may need to be procured that complies with local storage protocols. Hybrid solutions, combining on-premise and cloud-based storage, can be effective in managing costs and ensuring compliance with local storage protocols. We are seeing more customers opting for this data storage solution.

My advice is to include laboratory IT departments early and continuously throughout your digital journey. I believe it is fair to say that digital pathology vendors are supporting these storage challenges with novel solutions but that this will remain a relevant concern for labs into the future.

What measures might need to be introduced to ensure affordability and sustainability of digital pathology?

There is a trend for WSI scanners to be released to the market with greater and greater slide capacity. They are an expensive outlay and annual software subscriptions can mount up too. As with all lab investments it is important to consider the return on investment. Some of these returns can be tangible. The Digital Pathology Association has published a return on investment calculator for its members. It considers the upfront costs of procurement, project costs, staffing, training, and so on, offset against savings generated by digitization and revenue gains from bringing tests in house etc. It can be useful in business case discussions. Some pathology staining vendors are reducing the upfront financial barriers to digital pathology by offering laboratories solutions that see outlays blended into staining reagent rental programs.

Reimbursement of digital pathology has been slow and is very region specific. Advancements in this area would be welcomed since it would both reduce the overall cost and also stimulate the broader adoption of these technologies, to benefit patients.

Emerging technologies such as virtual staining have the potential to increase sustainability. Essentially, it uses algorithms to predict what staining would look like if it were to be undertaken on a tissue. It has multiple use cases, but a clear and obvious one that comes to mind is special staining. Here, algorithms run on an H&E image could be used to predict special stain outcomes, thus reducing reliance on the use of toxic chemicals, and ultimately reducing waste.

PROFESSION

Pathology as a Preference

Medical student Samantha Scetta reflects on the lab experiences that shaped her ambitions

By Samantha Scetta

The month was August, the year was 2021, and I was locked inside of a patient's upstairs apartment in the midst of a sweltering New England heatwave.

My patient: a 55-year-old febrile man, homebound, Spanish speaking. I had just extracted three tubes of blood from his right antecubital fossa and had a list of ten other patients to see before delivering his blood to the hospital for specimen processing. Now, I was crouched below his doorknob with a bobby pin in hand trying to channel my inner John Wick to escape the wrath of locked doors – and what I suspected to be a COVID-19 infection.

The patient was sitting at his kitchen table, apologizing profusely, as I tried to reconcile all of the ways this strange situation could have been worse. Finally, I heard the unmistakable click of the lock, gave the patient my pleasantries, and headed on out to bring his precious tubes of blood to the mini-centrifuge that had a permanent home in the trunk of my car.

As I finished up drawing blood from the remaining patients on my roster and headed back to the hospital, all I could think about was the events of the preceding morning. I had acquired a useful set of skills by working as a home-draw phlebotomist during the COVID-19 pandemic, with tactfulness climbing its way to the top of the list.

From specimen to analyzer

Although I had worked as a phlebotomist for several years during my undergraduate years and beyond, I decided I wanted to be involved in what happened with bodily fluids after they had, well, exited the body. This realization led me to years of involvement in pathology and laboratory science, and to a job where I had the opportunity to explore the inner workings of the hospital from the standpoint of the laboratory – where science and clinical skills come together.

I stumbled upon a job as a clinical laboratory assistant right around the time of the locked-in incident, and continued to work as a phlebotomist concurrently. This allowed me to see the entire journey of the specimen from patient to analyzer to lab results.

Eventually, I decided to dedicate my time to the clinical lab fully. Here, I worked in both clinical chemistry and hematology – two areas of the lab that helped me establish a firm foundation of clinical pathology before truly learning the pathophysiology of disease during medical school.

Discovering the microscopic world

To me, everything about the laboratory was novel and exciting… even years later. The way that instruments are treated like patients, with constant assessing of quality assurance and tending to hiccups, the rapidly changing advancements in technology, and of course, looking at peripheral blood smears under a microscope.

I remember spending quiet weekend afternoons with co-workers, identifying cell types for fun and looking at canonized cases of blood parasites and sickle cell anemia under the double-headed microscope. This was contrasted with the busy Friday nights, when we would receive hundreds of specimens from everywhere in the hospital and outpatient labs, triaging specimens in the same way that we would triage patients.

The medical laboratory scientists and technologists I worked amongst were incredibly well versed in lab values and pattern recognition, and their diligence and attention to detail inspire me to this day. As they introduced me to the microscopic world that exists within all of us, I became more affirmed that pathology and laboratory medicine was the perfect fit for me – a feeling that remained with me throughout medical school.

Back to the classroom

When I started medical school, I was fortunate enough to keep my job per-diem at the lab, and would work over holidays and long weekends. My experiences in the lab helped me with my studies in a practical and basic sense: knowing reference ranges, the components of a complete metabolic panel, and how to interpret a complete blood count on a rudimentary level. But, more than that, my experiences helped me understand the ways the laboratory elevates the hospital from the medieval days of medicine, when all a physician had was the physical examination to make an entire diagnosis and treatment plan.

Choosing laboratory medicine

It happens every time I'm asked the inevitable question by peers, physicians, family, and friends: "What field do you want to go into?" I tell them "pathology" and await the responses – ranging from inquisitiveness, through confusion, to thinly veiled revulsion.

Reactions of positivity and support tend to come from those who have had experience with the laboratory themselves. That says to me that we need to work together to unravel the mysteries that lie behind the doors of the laboratory for those that are in medical school and beyond. We need clinicians and students, alike, to appreciate the work behind the laboratory data and pathology reports that populate patients' charts across the country.

With technological intelligence slowly but surely being integrated into clinical informatics, pathology will likely change along with the rest of medicine. As physicians, we should be versed and interested in where the data and information that will be driving our clinical decisions comes from. Maybe these changes will cause the paradigm to shift, and we'll see people of varied backgrounds seeking out the laboratory – with intention and enthusiasm.

Samantha Scetta is a fourth-year osteopathic medical student at The University Of New England.

PROFESSION

Careers Uncovered: Pathology Informaticist

Matthew Hanna, Vice Chair Pathology Informatics at University of Pittsburgh Medical Center (UPMC), on modernizing workflows, managing change, and rising to challenges

What drew you to pathology?

My initial ambition was to become a surgeon. At medical school I took a few electives in surgery where I realised I was curious about what happened to my surgical specimens and what they could reveal about the downstream impact of my surgeries. So, thinking it would make me a better surgeon, I opted for an elective in pathology.

That elective exposed me to some amazing people and excellent mentors, and I was inspired by the mental gymnastics that I saw happening in the lab. While students are exposed to pathology in medical school, actually practicing it proved to be very eye opening.

One pathology elective led to another as I became more enamoured with the field. Pathology ended up as my first choice match for residency – and the rest is history.

"I want to fundamentally modernize pathology and the tools we use in its practice."

What led to you pursuing informatics?

When I started my residency, informatics didn't exist as a medical specialty. By the time I was thinking about fellowships, however, it had just become a board certified specialty, and it felt like a good fit for me.

That led me to UPMC, which had a strong reputation for its pathology informatics program. I was lucky enough to be mentored by Liron Pantanowitz, who might be described as one of the fathers of digital pathology.

How would you describe your work in lay terms?

All the computing and information systems we use in healthcare settings are developed, configured, deployed, and maintained by informaticists – so my job involves working with a lot of technology for the benefit of people's health.

I get to work with new technologies for both operational and clinical needs. We might be setting up and improving laboratory information systems, developing tools to help patients in need of care, or testing off-the-shelf solutions and putting them to work – and it's a lot of fun.

What's your favorite aspect of your work?

It's fun! And it matters.

In one of my pathology residency interviews, when asked what effect I wanted to have on pathology, my answer came easily: "I want to fundamentally modernize pathology and the tools we use in its practice."

Now I can reflect on my achievements and recognize that I have had, I hope, a small part to play in some of the larger advances in informatics and patient care. I can confidently say that the tools to truly modernize pathology are now available. Next, we need to persuade the pathology community to step onto the adoption curve.

What advice would you give to those who might want to follow in your footsteps?

We need more informaticists in general – and definitely in pathology. It's certainly a growth area in terms of employment, with great job security. It's a tremendous field for those with the skills to bridge the gap between clinical and technical needs, and liaise with the people on either side.

Sometimes the hardest things in life are the things most worth doing. Don't let anyone tell you in life that it is not that easy.

Read the full article online.


“Whatever it takes to get the most accurate diagnosis is worth it – because everything that follows depends on it.”

From Passion to Practice: A Life in Neuropathology

Sitting Down With… Daniel Brat, professor of neuropathology and lifetime educator

What first drew you to neuropathology, and how has your focus evolved over the years?
I was drawn to pathology – specifically neuropathology – fairly late in medical school. I've always been interested in the brain; my PhD was in neurobiology, focused on how neurons and their axons become dysfunctional. I was considering fields like neurology, neurosurgery, or psychiatry, but hadn't decided. Then a mentor at the Mayo Clinic suggested I try a rotation in neuropathology.

Within a few days, I knew it was the right fit. The people, the work – it all felt right. Neuropathology lets me study the brain and neurological diseases while also doing meaningful clinical and research work. It's a field that combines intellectual depth, high data intensity, and strong clinical impact. It's a very special field for those who are drawn to it.

In your view, what are the most pressing diagnostic challenges in surgical neuropathology today?
One of the biggest challenges is making sure diagnostic standards are adopted globally. We still need to be skilled at diagnosing disease under the microscope, but these additional tools have greatly improved what we can do.

In central nervous system tumors, some diagnoses are very complex and require advanced tests like methylation profiling. Unfortunately, not all institutions – or countries – have access to these tools. That creates a gap in diagnostic ability between high- and low-resource settings.

Each time a new WHO classification is released, it reflects advances in the field – most of which rely on molecular techniques. So, we're in a tough spot: we can offer the best diagnoses when we have access to these technologies, but many places still don't. We need better ways to help all pathologists, regardless of location, reach the same diagnostic standards.

What advice would you give to early-career anatomic pathologists interested in pursuing neuropathology?
You've already made a great decision by choosing pathology. Now within that field, choose something you're truly passionate about – you'll be doing this for decades, so it should be something you enjoy and care about deeply. If the brain interests you, go for neuropathology. It's the organ that defines who we are, and studying it is incredibly rewarding.

People who go into neuropathology are usually very passionate. You rarely hear someone say they regret it. In fact, many people transfer into pathology, not away from it. That's because choosing this path often requires deep thought and commitment – especially since it doesn't always match the typical image of a doctor that students have early on.

For many, deciding to go into pathology or neuropathology means stepping outside the mainstream of medical careers. It can feel like a bold move, but once you make that decision, it's freeing. You get to spend your career doing work you love. So if it feels right to you, don't hesitate – go for it.

What do you hope your legacy will be – as a diagnostician, teacher, and leader in the field of neuropathology?
I hope people see me as someone who had a real passion for neuropathology and wanted to share that passion and strive for excellence with everyone – students, trainees, colleagues, and faculty. I also hope that impact is recognized nationally and internationally.

I'd like to be remembered as someone who contributed, even in a small way, to advancing the field – especially in surgical neuropathology and the diagnosis of diffuse gliomas in adults. I've been lucky to work with great teams in pushing that forward.

Teaching is also a big part of who I am. I truly care about training residents and fellows, and I wouldn't want to be at an institution without them. I often joke that I started academic life at age four and never left – and I don't plan to. It's more than just work to me.

I recently watched the show Severance, where people split their work and personal lives completely. That's not me. I'm the same person in and out of work. My identity is tied to what I do, and I hope others can see and value that.

Any expectations or hopes for the future of neuropathology, or the pathology field as a whole?
I hope people continue to recognize how clinically important pathology – and especially neuropathology – is. Too often, it's seen as a "black box" that people don't fully understand, which leads to efforts to cut costs or treat it as separate from the rest of care.

I want there to be more awareness of what pathologists, neuropathologists, and our labs actually do every day. I often hear concerns about the rising cost of molecular testing, but when you look at the full picture – everything a patient with a brain tumor goes through, from imaging and doctor visits to surgery, radiation, and chemotherapy – the cost of molecular diagnostics is actually very small. In fact, most of those steps are leading up to one thing: getting a diagnosis. And that's our job. So whatever it takes to get the most accurate diagnosis is worth it – because everything that follows depends on it.

We shouldn't feel the need to apologize for the cost of doing high-quality diagnostic work. Instead, we should be proud of the value we bring and advocate for the tools we need to do our job well. The cost is modest, and the impact is huge.

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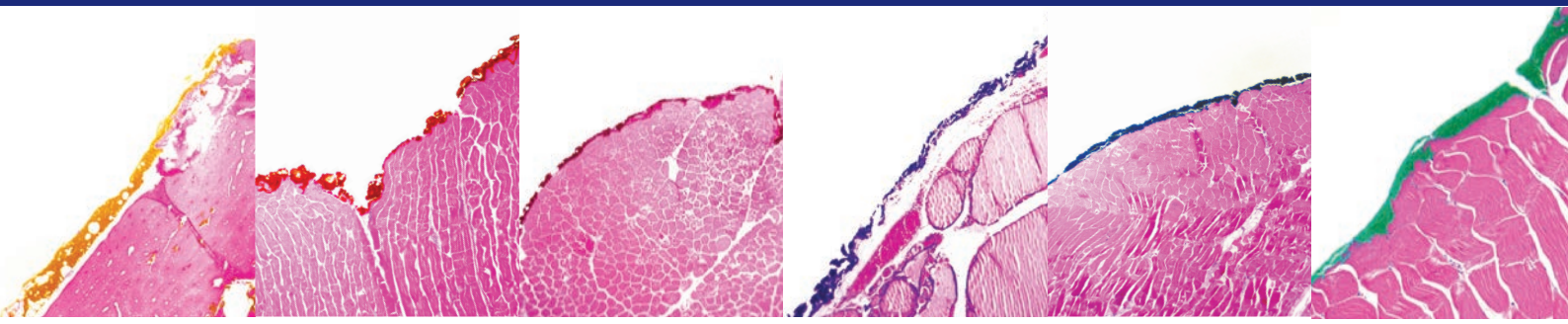

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