Clinician-Driven Test Development Supports Comprehensive Drug Panels

Pain Panel (6-acetylmorphine)

Relative abundance

Time (min)

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Pain management drugs and benzodiazepines are among the most prescribed medications, and they are also the most abused classes of prescription drugs.\(^1\) Patients enrolled in pain management programs must be monitored for compliance, which means appropriate use of prescribed drugs and abstinence from non-prescribed drugs.

Laboratory medicine supports this public health effort with comprehensive panels that detect and measure the presence of a number of drugs or their metabolites in the patient's urine. Although opioid medications such as fentanyl, oxycodone (OxyContin, Percocet), and hydrocodone (Vicodin) are often targeted, benzodiazepines such as diazepam (Valium) and alprazolam (Xanax) also have a high risk for abuse or other negative interactions, and they should be monitored as well.

At Cleveland Clinic's Robert J. Tomsich Pathology & Laboratory Medicine Institute (RT-PLMI), the development of these panels has been guided by active collaboration between laboratory medical and administrative staff and practicing physicians from a variety of fields, including pain management, addiction and recovery, and behavioral health. Representing RT-PLMI in this interdisciplinary work group are:

- Sihe Wang, PhD, section head of clinical biochemistry
- Adam McShane, PhD, clinical biochemistry fellow
- Dustin Bunch, PhD, development technologist
- Courtney Heideloff, supervisor of family health center – central region
- Drew Payto, supervisor of special chemistry

This innovative clinician-driven model seeks to develop tests that are the most appropriate and cost effective tests for the specific drugs that physicians encounter in regular clinical practice, without performing unnecessary or duplicative procedures. As described by Xavier Jimenez, MD, director of the Chronic Pain Rehabilitation Program in Cleveland Clinic's Neurological Institute and one of the practitioners in the group, “How can we maximize the laboratory's resources, personnel, and procedures to help what we're doing clinically?”

**The Need for Comprehensive Testing**

A 2012 National Health Interview Study found that 25.5 million adults reported suffering from chronic or daily pain, and 39.8 million adults (or 17.6% of all adults) had recently experienced category 3 or 4 pain, the highest levels on the study’s scale.\(^4\) The same year, there were 259 million prescriptions for opioid pain relievers written in the United States, following a 7.3% increase in prescription rate from 2007.\(^5\)

Benzodiazepines are widely prescribed to treat anxiety, sleep disorders, seizures, or muscle spasms. In 2008, approximately 75 million benzodiazepine prescriptions were filled in the United States.\(^3\)

Laboratory testing helps maintain patient safety when prescribing these powerful medications. In addition to the potential for addiction with both opioids and benzodiazepines, these classes of drugs also should not be taken together, as their combined use greatly increases the risk of respiratory depression and other serious complications. To safeguard against this dangerous combination, clinicians treating patients on an opioid pain management program may also run a panel to check for benzodiazepines, or vice versa.

“We want to give the appropriate medications for patients who are in pain and need treatment, and we need to do it carefully to maintain patient safety,” says Beth Minzter, MD, medical director for Pain Management for Cleveland Clinic main campus and a staff physician in the Anesthesiology Institute. For several years, Dr. Minzter has worked with Dr. Wang and his group on these tests to meet the needs of pain management programs. “Clinicians want to prescribe as safely as possible, and these tests help us make the best clinical decisions for our patients.”
Narrowing the Field
With dozens of opioid and benzodiazepine medications on the market, it is crucial to narrow the number of analytes. Limiting the number of substances being targeted in each panel helps contain costs and turnaround times—an important consideration for tests that often require being reordered periodically for compliance in pain management or rehabilitation programs. A leaner list also improves ease of use and clinical interpretation of test results.

“We knew that if the tests were overly complex or expensive, they wouldn’t be used. Making the tests clinically useful was our primary goal,” explains David Streem, MD, medical director of the Alcohol and Drug Recovery Center at Cleveland Clinic Lutheran Hospital. Dr. Streem has also worked with RT-PLMI on drug test development.

With this in mind, the developers focused on the drugs that are most commonly used or abused in a treatment or rehabilitation setting, relying heavily on the practical experience of the clinicians in the group. Likewise, Dr. Wang and Dr. McShane advised on the chemistry involved in testing a multiplicity of related analytes.

The combination of laboratory science and clinical practice helped reconcile the broad scope of what is scientifically possible with what is most clinically useful. After much informed discussion, the pain management panel was limited to 11 prescription medications (and related metabolites) and 5 illegal drugs, and the benzodiazepine panel was honed down to 7 medications. (See Table.)

Methodology Matters
The methodologies selected for comprehensive drug panels also have a definite impact on the amount of information that clinicians can gain from the tests.

For analysis, providers may initially consider immunoassays because of their quick turnaround, convenience, and relatively low cost, but this testing method has several critical limitations. Immunoassays may lack the needed analytical sensitivity and/or specificity. For opioids, most immunoassay tests cannot distinguish between various specific drugs and cannot detect oxymorphone at all. For benzodiazepines, most immunoassay tests have unacceptable false-negative and false-positive rates for various benzodiazepines. In addition, immunoassays are commonly only semi-quantitative, and clinicians in some cases need quantitative assessment of urine drug concentrations.

In practice, the limitations of immunoassays can translate into serious consequences for patients. “In recovery programs, lab tests are used to prove patients’ treatment success and sobriety, and a false positive can bring that all into question,” says Dr. Streem. “For many patients, there’s a lot at stake.”

Additionally, certain drugs may actually be prescribed as part of a treatment plan, such as buprenorphine which may be used to treat opioid addiction. A qualitative immunoassay may not allow the provider to determine whether the substance detected in the patient’s urine is

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**Quantitative Pain Panel Analytes**
- Morphine
- Codeine
- Dihydrocodeine
- Oxycodone
- Oxymorphone
- Hydrocodone
- Hydromorphone
- Methadone and metabolite (EDDP)
- Fentanyl and metabolite (Norfentanyl)
- Tramadol and metabolite (O-Desmethyltramadol)
- Buprenorphine and metabolite (Norbuprenorphine)
- Amphetamine
- Methamphetamine
- Cocaine metabolite (Benzoylecgonine)
- Heroin metabolite (6-Acetylmorphine)
- Marijuana metabolite (THCA)

**Benzodiazepine Panel Analytes**
- Nordiazepam
- Temazepam
- Oxazepam
- Lorazepam
- Alpha-hydroxalprazolam
- Alpha-hydroxytriazolam
- 7-Amino-clonazepam

| Table. List of analytes in pain management and benzodiazepine panels |
an appropriately prescribed medication or some related drug that is prohibited.

In contrast to immunoassays, high performance liquid chromatography tandem mass spectrometry (HPLC-MS/MS) offers high resolving power, high selectivity, and wide dynamic range, all of which enable simultaneous quantification of a broad spectrum of drugs present in biological matrices. Recent research recommends the use of LC-MS/MS to measure opioids and benzodiazepines due to the method’s high sensitivity and specificity.

Another consideration is the hydrolysis method used to convert drugs conjugated with glucuronide in urine specimens back into free drugs. The conjugation rate varies significantly within and among patients, and so conjugated drugs are usually converted to free drugs prior to analysis for more consistent results. This includes opiates such as morphine and codeine, or benzodiazepines such as oxazepam, lorazepam, and temazepam.

Chemical hydrolysis is efficient but may result in unwanted reactions. For example, acid hydrolysis can cause structural changes to various benzodiazepines, leading to a loss of compound information which can obscure the original benzodiazepine. In contrast, enzymatic hydrolysis is much milder and is better at identifying the original drug, but it needs longer incubation times to achieve sufficient hydrolysis efficiency.

Interpretation and Communication

Even with drug panels designed for simplicity and accuracy, the complexity of factors affecting the test’s results may make interpretation more challenging than a simple positive/negative test. For example, the level of drugs or metabolites discovered in urine can vary due to many factors, including dosage, the patient’s individual metabolic rate and hydration status, and the relative time between drug use and collection of the urine sample. The presence of other medications or substances, prescribed or otherwise, can also affect test results.

For pain management and benzodiazepine panels at Cleveland Clinic, results are provided in a detailed report with interpretive comments written by laboratory staff who are knowledgeable of the chemistry involved in each analyte as well as any possible interactions. Additional consultative support for results interpretation is available as needed.

"In a clinical setting, interpreting someone’s test results isn’t always straightforward," says Dr. Streem, who often has to try to deduce a patient’s usage behavior from the quantitative values in the test report. "If I have questions about the results, laboratory staff are always available to help understand the nuances of the test."

Dr. Minzter echoes this sentiment, adding, “Dr. Wang and his staff in RT-PLMI are excellent at explaining test results and putting them into proper context. We can use the objective data from these tests and make informed, independent clinical decisions for our patients.”

Putting Patient Success First

Although drug panels are usually performed to monitor possible abuse or diversion of drugs, clinicians emphasize the value of testing in contributing to the patient’s treatment success. Accurate and objective test results, expert interpretation, and informed clinical decision-making allow patients who are appropriately using prescription medications to continue doing so. That means that Dr. Jimenez and Dr. Streem’s patients can continue participating and making progress in their recovery programs, and physicians such as Dr. Minzter can continue prescribing the appropriate medications that bring relief to patients who are in great pain.

This focus on patient success has made the development of these tests a positive, productive process. As Dr. Wang in RT-PLMI notes, “This has been one of the best experiences. Everyone has been engaged, with a unified purpose.”

By incorporating clinicians from a variety of institutional backgrounds into the test development process, these comprehensive panels have been developed with a distinct appreciation for how drug tests are used in daily practice and how they can have a significant impact on a patient’s treatment success.
References


Merkel cell carcinoma, also known as neuroendocrine carcinoma of the skin, is a cancer comprised of touch receptor cells in the epidermis called Merkel cells. Merkel cell carcinoma is a relatively rare form of skin cancer with about 1,500 cases per year, compared to melanoma which is 40 times more common. However, Merkel cell carcinoma is especially aggressive and lethal, and it can metastasize quickly via the lymphatic system.

Biopsy of the sentinel (first) tumor draining lymph node is a prognostic tool that has revolutionized the staging and treatment of a number of common cancers, including breast cancer and malignant melanoma, and it has also been used for Merkel cell carcinoma. This procedure allows for more accurate identification of tumor micrometastases in tumor draining lymph nodes. Scientific studies have shown that the amount of tumor burden observed in the sentinel lymph node further refines prognosis in breast cancer and melanoma. As such, rare tumor cells do not carry clinical significance in breast cancer, and thus lead to a separate clinical staging annotation in patients, given the uniquely reduced risk. In melanoma, however, it is known that even rare tumor cells carry prognostic significance.

Because Merkel cell carcinoma has been relatively rare (although the incidence is increasing), the prognostic significance of variable amounts and patterns of tumor found in the sentinel lymph node was previously unexplored. In a study of 64 cases of sentinel lymph node biopsies involving Merkel cell carcinoma, researchers hypothesized that the histological pattern of cancer cells observed in sentinel lymph node biopsies may impact Merkel cell carcinoma prognosis, and that this factor could more precisely stratify expected outcomes for patients with stage III Merkel cell cancers, helping to guide treatment options and expectations with greater specificity.

Our researchers observed 5 different histological patterns of lymph node involvement. The most common pattern featured a solid, sheet-like proliferation of metastatic tumor cells with variable amounts of lymph node parenchyma, and this pattern was associated with overall worse survival than any of the other four patterns. Furthermore, there was no significant difference of survival among the other four patterns, allowing all five patterns to be distinguished into two main categories: pattern 1 (solid, sheet-like) or non-pattern 1 (non-solid parafollicular, sinusoidal, perivascular hilar, or scattered parenchymal) (Figure 1). In other words, if a patient’s sentinel lymph node biopsy revealed the pattern 1 sheet-like arrangement of cancer cells, he or she would have a lower expected 2-year survival rate compared to a patient with any other pattern of Merkel cell carcinoma.

In addition to the sentinel lymph node pattern, other significant factors were found to be associated with

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Figure 1. Merkel cell carcinoma histological patterns in sentinel lymph node: (a) solid, sheet-like, (b) non-solid parafollicular, (c) sinusoidal, (d) perivascular hilar, and (e) scattered parenchymal.
expected patient outcomes for Merkel cell carcinoma. Patients with 2 or more MCC-positive sentinel lymph nodes had poorer survival (Figure 2), and older patients (70 years or older) also fared worse. Merkel cell carcinoma is known to be associated with Merkel cell polyomavirus, and so patients with compromised or suppressed immune systems—due to either a comorbidity or medication associated with immune suppression—also had poorer survival than immunocompetent patients. By weighting and combining all of these factors associated with survival outcomes, stage III patients (patients with any amount of tumor within their sentinel lymph node) with Merkel cell carcinoma can be characterized into one of three prognostic groups: Favorable, Intermediate, or Unfavorable.

There are significant differences in survival rates between the Favorable, Intermediate, and Unfavorable groups (Figure 3). Patients in the Favorable group (those with patterns 2-5 and only 1 or 2 positive sentinel lymph nodes) experienced very good 2-year survival of 90%, and patients in the Intermediate group (those with one or more poor features including pattern 1 SLN biopsies, advanced age ≥70, or immunosuppression) had a 2-year survival of 73%. In the Unfavorable group (including patients with additional poor features), none of the patients survived within 2 years of diagnosis.

Based on these clear survival differences, these prognostic groups allow for additional stratification not previously available for Merkel cell carcinomas. As of 2010, Merkel cell carcinoma has been staged using the basic 4-stage system based on the primary tumor size (less than 2 cm for stage I and greater than 2 cm for stage II), the presence of disease in lymph nodes (stage III), and the spread of distant metastasis (stage IV).

In 2016, this staging system was revised, with additional stratifications based on whether the cancer was staged clinically or pathologically, whether a primary tumor was detected, and whether regional nodal disease was detected with in-transit metastases. However, even within these substages, the prognostic indications for survival can vary greatly. Using the 3 prognostic groups based on histological patterns could provide physicians with additional information to guide treatment options. For example, physicians may choose more aggressive treatments for Merkel cell carcinomas in the Unfavorable group exhibiting pattern 1 (solid sheet-like) arrangements, since they are associated with worse outcomes than any other pattern.

The study of histological patterns of Merkel cell carcinoma also provides additional insight into the imaging techniques used in sentinel lymph node biopsy. Because of their diffuse concentration of metastasis, pattern 1 (solid, sheet-like) carcinomas can be detected even with less sensitive H&E stains, while detection of patterns 2-5 depends more heavily on immunohistochemistry’s ability to reveal more diffuse or isolated tumor cells. Since the tumors most heavily associated with negative outcomes can be detected from H&E stains alone, pathologists may consider using such methods for detecting Merkel cell carcinoma for diagnosis and prognosis, while more sensitive immunohistochemical methods can be reserved for confirmation.

Examination of Merkel cell carcinoma cell patterning leads to several recommendations for prognosis and treatment. As noted, in most cases standard H&E stains are sufficient to develop a meaningful prognosis of expected outcome, since that technique is able to detect the solid, sheet-like histological pattern known to be associated with worse outcomes. Additionally, advanced age and
immunosuppression play a distinct role in prognosis of Merkel cell carcinoma, as both factors have been shown to negatively affect outcome. If the sentinel lymph node biopsy does reveal the more dangerous solid, sheet-like pattern, physicians could recommend more aggressive treatment, all the more so for older patients (>70 years old) or patients with compromised immune systems.

Treatment options for Merkel cell carcinoma are similar to those for other skin cancers, with surgical excision, radiation, and chemotherapy being typical treatments.7 Surgery can be used to remove both the primary site of the Merkel cell carcinoma and the positive local lymph nodes, and it is recommended to perform the sentinel lymph node biopsy prior to or at the time of the excision surgery.8 Surgery alone may be successful for lower risk MCC tumors, but for higher risk cases of Merkel cell carcinoma, radiation therapy performed in conjunction with surgery has been shown to greatly decrease the risk of recurrence, especially in local cases. There is still some controversy, however, as to how effective adjuvant radiation therapy is to both local recurrence and distant metastasis.9 Additional studies are needed to confirm the exact advantage of adjuvant radiation therapy, but there is indication that this combination therapy could be appropriate for higher-risk patients such as those associated with pattern-1 sentinel lymph node biopsy or the non-Favorable prognostic groups.

Chemotherapy for Merkel cell carcinoma has been shown to be effective initially in reducing tumors, but its long-term effects are not durable and MCC can actually develop resistance to the chemotherapy drugs.6 Chemotherapy is usually reserved for palliative treatment of late-stage metastatic Merkel cell cancers, which could include patients identified in the Unfavorable prognostic group based on sentinel lymph node biopsy pattern and other poor features.

As an especially aggressive and lethal form of skin cancer, expected outcomes for Merkel cell carcinoma tend to be unfavorable. The information gained from sentinel lymph node biopsies can provide more precise and useful prognostic information for physicians and patients to work with, indicating appropriate methods and treatments based on the proliferation and pattern of the patient’s cancer cells as well as the other contributing factors.

References
About the Author

Jennifer S. Ko, MD, PhD

Jennifer S. Ko, MD, PhD, is a staff dermatopathologist in Anatomic Pathology and Dermatopathology at Cleveland Clinic. She is also the medical director of the Cleveland Clinic Central Biorepository and is a clinical assistant professor of pathology at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University.

Dr. Ko joined Cleveland Clinic in 2003 after completing a 6-year BS/MD program at Northeastern Ohio Universities College of Medicine (now Northeast Ohio Medical University). She completed a 1-year residency internship in internal medicine and then completed a PhD in immunology from Case Western Reserve University.

During her PhD training, Dr. Ko worked in the Lerner Research Institute, studying cancer induced immune suppression and immune therapy for cancer. She also worked as a clinical scholar in the Taussig Cancer Institute, caring for patients with melanoma, Merkel cell carcinoma, and other advanced skin cancers. Dr. Ko did her subsequent residency in anatomic and clinical pathology and fellowship training in dermatopathology at Cleveland Clinic.

Dr. Ko has authored numerous publications and scientific presentations and is the recipient of several research awards and scholarships. Dr. Ko's personal research interests include melanoma and pigmented lesion diagnosis, Merkel cell carcinoma, immune suppression in cancer, and identifying novel immunotherapeutic targets in melanoma. She also enjoys working closely with clinical and scientific researchers throughout Cleveland Clinic/Lerner Research Institute on translational research projects that require the support of the Central Biorepository. Dr. Ko can be contacted at 216.965.5134 or koj2@ccf.org.
Histology of Joint Implant Failures and Bone Graft Materials

By Thomas W. Bauer, MD, PhD

Total joint replacement surgery is a common and generally successful procedure, with nearly 7 million people in the United States living with a hip or knee replacement. However, prosthetic failures occur in approximately 1-2% of arthroplasty cases, and can be associated with damage to periprosthetic tissues and inflammation. Similarly, material from bone grafts and synthetic bone graft substitutes can result in histological abnormalities that pathologists either may not recognize or may misinterpret as necrotic lesion tissue. In both cases, recognition of characteristic histological reactions caused by implant failures can help guide clinical diagnosis and treatment, provide information for improved device manufacture, and maintain compliance with federal reporting policies.

Implant Failures
There are many potential mechanisms of arthroplasty failure, but those of most interest to pathologists include: insufficient osseointegration, osteolysis, periprosthetic joint infection (PJI), aseptic lymphocyte dominant vasculitis-associated lesion (ALVAL), and pseudotumors.

Insufficient osseointegration – If an implanted device does not adequately bond with the bone, then micromotion may induce a fibrous membrane or granulation tissue. Imaging reveals a linear radiolucency around the implant, and histology of the peri-implant tissue shows a fibrous membrane with no neutrophils and relatively few macrophages. Particles of wear debris, giant cells, lymphocytes, and plasma cells are also rare.

Osteolysis – A macrophage and giant cell reaction to implant wear debris particles can induce osteoclasts to resorb bone (“osteolysis”), contributing to implant loosening and pain. Biopsies show sheets of macrophages with a foamy or granular-appearing cytoplasm created by debris particles (Figure 1). Necrosis can be prominent but with relatively few lymphocytes. Debris particles from arthroplasty wear or failure may also be observed in regional or distant lymph nodes due to migration of the particles via the lymphatic system.

Periprosthetic joint infection (PJI) – Infection around the joint implant, or periprosthetic joint infection (PJI), is one of the most common and serious complications of total joint replacement, and it can result in considerable healthcare costs and patient distress. Diagnostic guidelines from the American Academy of Orthopedic Surgeons (AAOS) recommend intraoperative consultations (frozen sections) in cases where periprosthetic infection has been neither diagnosed nor excluded. The AAOS found adequate literature to support two different thresholds for diagnosing infection: (1) a maximum tissue concentration of 5 neutrophils in each of five, ×400 high power fields (hpf), or (2) 10 neutrophils in each of 5 hpf. Cleveland Clinic looks for a more sensitive reading of at least 5 neutrophils in each of 3 hpf.

Neutrophils beneath the surface of the membrane are suggestive of infection (Figure 2), but neutrophils entrapped in superficial fibrin, blood clot, bone marrow, or within vessels are not considered to be diagnostic. Additionally, lymphocytes and plasma cells are not considered indicative of PJI. Frozen sections can be more difficult to interpret and diagnose due to cauterization from surgery, or inflammation from other conditions such as rheumatoid arthritis.
Aseptic lymphocyte dominant vasculitis-associated lesion (ALVAL) – An unusual pattern of inflammation associated with failures of metal-on-metal implants and devices with corrosion at modular interfaces has been termed “aseptic lymphocyte dominant vasculitis-associated lesion” (ALVAL), and consists of a laminated fibrous membrane with superficial necrosis, a hyalinized layer of collagen just beneath the surface, and deeper perivascular and diffusely distributed chronic inflammation (Figure 3).\textsuperscript{11,12} Particles in macrophages may have a green, grey-green, or brown appearance. Despite its name, ALVAL is not a true vasculitis; the inflammation is thought by many investigators to reflect an immune reaction to metal particles or ions.

Pseudotumors – Solid or cystic mass lesions around the hip may be observed with failed metal-on-metal implants or devices with corrosion at modular junctions.\textsuperscript{13-17} Sometimes referred to as “pseudotumors,” such lesions may be associated with inflammation similar to ALVAL. Additional studies are needed to establish more rigorous criteria for this designation as well as the mechanism causing the lesions.

Bone Graft Materials

Bone grafts used to replace bone tissue around sites of previously failed implants, fracture repair, or other orthopedic procedures employ a variety of materials that may not be recognized if observed in tissue sampled during subsequent operations.

Bone graft preparations – Autograft and allograft preparations can consist of bone fragments, bone marrow, stem cells, or connective tissue precursors, all of which can be misinterpreted as necrotic host tissue. Tissue that appears necrotic at the site of a previous orthopedic operation may in fact be bone fragments from bone graft used in the previous operation.

Demineralized bone matrix (DBM) – Commercially produced demineralized bone matrix (DBM) is used to induce bone formation, and in histology sections it can be recognized as shavings of cortical bone with empty osteocyte lacunae (Figure 4), sometimes associated with endochondral or intramembranous bone formation.

Synthetic calcium compounds – Compounds containing calcium and phosphate or sulphate used in bone graft substitutes may dissolve in specimen processing if subjected to decalcification, leaving observable voids in the section (Figure 5).\textsuperscript{18} The rate at which the compounds dissolve depends on their composition, with calcium sulphates generally dissolving faster than calcium phosphates.

Bone graft materials should not induce acute inflammation, so a high concentration of neutrophils associated with a bone graft material suggests the possibility of infection.
References


About the Author

Thomas W. Bauer, MD, PhD

Dr. Bauer has been a pathologist at Cleveland Clinic since 1983. He specializes in orthopaedic pathology, especially biomaterials, and in that context has published more than 245 peer-reviewed publications and 32 book chapters. He is the deputy editor for research for the Journal of Bone and Joint Surgery, is the co-editor-in-chief of JBJS Case Connector, has been a consultant to orthopaedic device manufacturers, and is a frequent speaker at orthopaedic and biomedical engineering meetings. He has been the medical director for the Center for ePathology since 2011. In his spare time during the last 10 years, he has completed more than 40 marathon races, five 50K races, six 50-mile and nine 100-mile ultramarathons.
News

Strong Presence for Cleveland Clinic at CAP16

The Cleveland Clinic Robert J. Tomsich Pathology & Laboratory Medicine Institute was well represented at the annual meeting of the College of American Pathologists (CAP), September 24-28, 2016, in Las Vegas, NV. Presenting regular conference sessions were: Fadi W. Abdul-Karim, MD, MEd; Steven Billings, MD; David Bosler, MD; John Goldblum, MD; Walter Henricks III, MD; Jonathan Myles, MD; Deepa Patil, MD; Gary Procop, MD; and Brian Rubin, MD, PhD.

Additionally, Carol Farver, MD, and Jordan Reynolds, MD, presented a fully booked pre-conference industry workshop on the topic of “Diagnosis of lung cancer using integrated histologic, cytologic, and molecular approaches in the era of precision medicine.”

In this discussion on non-small cell lung cancers (NSCLC), Dr. Farver and Dr. Reynolds defined the current required molecular testing for NSCLC, discussed Cleveland Clinic’s approach to testing NSCLC to determine cell type, and reviewed how our laboratories triage and optimize the handling of small specimens for diagnosis and therapy.
Alumni Connect

We are honored to feature one of our distinguished alumni, Jonathan L. Myles, MD, in this installment of Alumni Connect. Dr. Myles graduated from the Medical College of Ohio in 1983. After completing combined residencies in anatomic and clinical pathology at The Cleveland Clinic in 1987, he joined the faculty of the Medical College of Ohio (now University of Toledo Medical Center), where he achieved the rank of associate professor before being recruited back to Cleveland Clinic in 1993. He has served in a variety of roles in the Robert J. Tomsich Pathology & Laboratory Medicine Institute and currently serves as Director of Quality Assurance and CPT Coding in Anatomic Pathology. Dr. Myles participates in the genitourinary, breast, medical kidney, and cardiovascular pathology subspecialty services at Cleveland Clinic.

Dr. Myles is a national leader in pathology payment policy. He has served as the pathology advisor to the AMA-RUC (American Medical Association Relative Value Update Committee) since 2006. That committee recommends to CMS the relative value units for physician services. Dr. Myles has served as chair of the Economic Affairs Committee of the College of American Pathologists (CAP) since 2010. He is a member of the CAP Spokespersons Network and has served as faculty at the Engaged Leadership Academy of the CAP. He has served on the Board of Directors of the Academy of Medicine of Cleveland. Dr. Myles has received the CAP’s Public Service Award (the College’s highest honor related to public service) as well as the CAP’s Outstanding Service Award for his many years advocating for pathologists with both private and governmental agencies.

Dr. Myles has served as past president of the Ohio Society of Pathologists and Cleveland Society of Pathologists.

We recently had the opportunity to ask Dr. Myles to reflect on his training at Cleveland Clinic: “The best things about my training at the Cleveland Clinic were my fellow residents and the staff physicians who trained me. My mentors such as Drs. Howard S. Levin and Bruce A. Sebek inspired me to become the best possible pathologist I could and served as role models in my service to our patients. Dr. Robert S. Galen inspired me to use all the resources available to solve a difficult clinical chemistry issue and recognize that as a pathologist I am an integral part of the patient’s healthcare team. Dr. William R. Hart taught me what questions that you need to ask before making a decision. Cleveland Clinic’s residency program is large and that allowed me to learn from others residents such as Dr. Charles V. Biscotti who continues to give me guidance as a colleague today. My mentors always inspired me to do my best and encouraged my participation in local and national residency paper competitions. Our visiting professors made an impression that has lasted throughout my career. I recall Dr. Fathollah K. Mostofi being a visiting a professor and stating two things are needed to diagnose prostate cancer: cytologic atypia and architectural atypia. That one comment has served me for 30 years as an attending physician.”

We asked Dr. Myles why he is active in professional activities outside of his patient care responsibilities at Cleveland Clinic: “It is important for patient care that pathology maintains its leading role in medicine. The laboratory drives most medical decision-making by our clinical colleagues, and a less than precise diagnosis not only impacts patient treatment, but increases cost to the healthcare system. The viability of our specialty depends on receiving appropriate compensation for our services. I am currently a candidate for the College of American
Pathologists Board of Governors. In that role, I want to ensure that future generations of pathologists will have the same opportunities that I have to participate as a member of the healthcare team.”

“I want to ensure that future generations of pathologists will have the same opportunities that I have to participate as a member of the healthcare team.”

— Jonathan L. Myles, MD

For the past six years I have served as the pathology speciality director to the Alumni Board. The best part of my role has been to re-connect with you, our alumni. We have updated the contact information for all alumni where possible and have instituted the Article of the Week, which strengthens our connection. As a member of the Alumni Board, I have had the opportunity to meet new leaders at Cleveland Clinic as well as interact with old friends. Thank you for your support during my tenure as your representative."

We would like to thank Dr. Myles for his immense and much appreciated efforts in his role as pathology speciality director to the Alumni Board. He is leaving this role in late 2016, and we wish him all the best in his new endeavors. We welcome Dr. Christine Booth as she assumes the role of pathology speciality director to the Alumni Board, and we look forward to her service for our alumni.

We want to hear from you

Please send us your news and accomplishments to be featured in this “Alumni Connect” section in future issues of Pathology Today. If you prefer to receive an electronic version, please let us know by providing your preferred email address to ClientServices@ccf.org.

Fadi W. Abdul-Karim, MD, MEd
Vice-Chair, RT-PLMI
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Here you will find our test directory, technical briefs, technical updates, policies and procedures, specimen collection centers, and contact information.

Our website also features literature and publications, including current and past issues of Pathology Today, news articles, Pathology Insights videos, and white papers on current topics. Department information, a staff directory, and laboratory career opportunities can be found here, too.

News

Daniela Allende, MD, invited to Women’s Professional Staff Accelerated Development Program

Daniela Allende, MD, was selected to participate in the inaugural offering of the Women’s Professional Staff Accelerated Development Program, a new initiative from the Cleveland Clinic Global Leadership and Learning Institute. This accelerated program was built to help women physician leaders grow in the organization by focusing on key topics such as leadership, communication, team building, finance, and continuous improvement.

Dr. Allende was nominated for the program by RT-PLMI administration in recognition of her leadership within Cleveland Clinic, currently serving as Director of Hepatobiliary Pathology in the department of Anatomic Pathology. Through intense three-day sessions over three months, Dr. Allende will engage with other women leaders in highly interactive sessions conducted by noted leaders from both inside and outside of Cleveland Clinic.

“I am honored to be part of this amazing group and excited for all the things to come,” says Dr. Allende. “I am confident that the skills I will be learning throughout this program will provide the foundation to foster professional development among my peers and nurture the team-driven environment we all embrace in RT-PLMI.”

Cleveland Clinic Hosts Multispecialty Pathology Symposium in Las Vegas

The Cleveland Clinic Robert J. Tomsich Pathology & Laboratory Medicine Institute hosted the second annual Multispecialty Pathology Symposium, January 20-22, in Las Vegas, NV. Directed by Anatomic Pathology faculty John Goldblum, MD, and Cristina Magi-Galluzzi, MD, PhD, the well-attended conference featured practical discussions and expert analysis of commonly encountered dilemmas in surgical pathology and cytology. Also representing the Cleveland Clinic Department of Anatomic Pathology were Tarik Elsheikh, MD; Carol Farver, MD; and Deepa Patil, MD.

Attendees included a range of practicing pathologists, fellows, and residents, who attended nearly two dozen sessions on a range of topics in soft tissue, gastrointestinal, genitourinary, head and neck, cytology, and lung pathology.

“This symposium has been a great way to share Cleveland Clinic’s subspecialty experience with a wider community of pathologists,” said Dr. John Goldblum. “It’s been a pleasure to meet practitioners from across the country and help them recognize, diagnose, and manage these challenging cases.”

Look for information on next year’s Multispecialty Pathology Symposium, which is also planned for early spring in Las Vegas.
New Staff

Erinn Downs-Kelly, DO
Breast, Gastrointestinal Pathology

Maria Luisa C. Policarpio-Nicolas, MD
Cytology, Gynecologic Pathology

Daniel H. Farkas, PhD, HCLD
Section Head, Molecular Pathology

Erica Savage, MD
Gastrointestinal, Hepatobiliary Pathology

Scott Kilpatrick, MD
Bone and Soft Tissue Pathology, Cytopathology

Akeesha Shah, MD
Cytopathology, Head and Neck, and Endocrine Pathology