Scientific and Social Program, Speaker Biographies, Abstracts

ACLPS 2023

Annual Meeting

8-10 June 2023

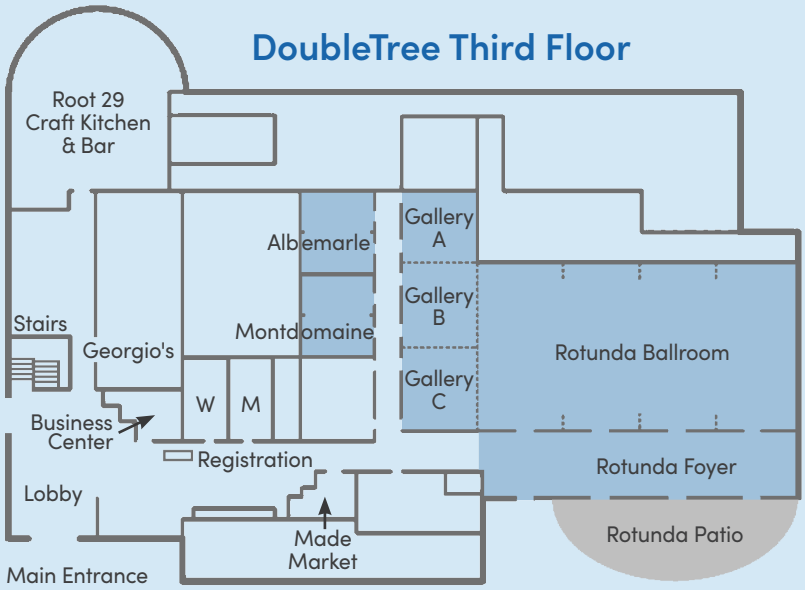
DoubleTree by Hilton Hotel

Charlottesville, Virginia

Organized by the

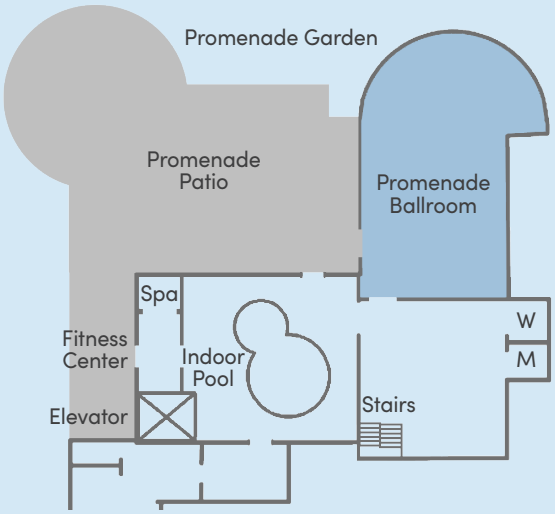
University of Virginia Department of Pathology

DoubleTree Third Floor



Scientific Sessions: Rotunda Ballroom
Abstract Breakouts: Gallery A-C, Albemarle, Montdomaine
Posters and Exhibits: Rotunda Foyer
Catering: Rotunda Foyer
Welcome Reception: Promenade Ballroom and Patio

DoubleTree First Floor



Contents

ACLPS

Advancing teaching and scholarship in Laboratory Medicine since 1966

www.aclps.org

Welcome, ACLPS23 Attendees!

The Department of Pathology at the University of Virginia School of Medicine welcomes you to the Annual Meeting of the Academy of Clinical Laboratory Physicians and Scientists. We are indeed honored to be your hosts for ACLPS23.

For early birds arriving on Wednesday, we have arranged for shuttles to take you from the Conference hotel, the DoubleTree, to the UVA grounds and/or to downtown Charlottesville. UVA's clinical chemistry fellow, Mark Girton, will be providing personalized guided tours of central grounds, including the famous Rotunda that oversees UVA's "Academical Village."

Thursday is chock-full of exciting seminars given by leaders and experts in Laboratory Medicine. The day's sessions close with a short presentation by Columbia's Department of Pathology and Laboratory Medicine, to introduce you to ACLPS24, taking place in the Big Apple. The Thursday night Welcome Reception will be held in the Promenade Ballroom at the DoubleTree.

Friday morning, the Young Investigator Oral parallel Abstract presentations will take place in various conference rooms at the DoubleTree, with ample signage to help you find your sessions. YI Poster sessions will take place in the Rotunda Foyer. At noon, the ACLPS Business Meeting (with lunch) will take place in the Rotunda ballroom. Next, we will hear from UVA's own Amy Mathers, this year's awardee of the Ernest Cotlove Award Lectureship. You will not want to miss her timely and exciting talk "The 'next' pandemic – antibacterial resistance."

Shuttles will begin to leave the DoubleTree at 5:20 pm to bring you to the Cocktail Hour and Awards Banquet at Montalto (the "high mountain") that is part of Thomas Jefferson's historic estate, Monticello. Repose, the 11,000-square-foot house atop Montalto, is a gracious 1908 American Country house restored by the Thomas Jefferson Foundation in 2011. It is an event destination with sweeping views of Charlottesville and the Blue Ridge Mountains. Be sure to enjoy signature Blue and Orange Cocktails, representing the colors of UVA, founded by Mr. Jefferson.

ACLPS23 Planning Committee

UNIVERSITY of VIRGINIA | SCHOOL of MEDICINE

Co-Chairs

James Gorham, MD, PhD

Lindsay Bazydlo, PhD, DABCC, FAACC

Committee Members

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Jinbo Fan, PhD

Tonya Gomez

Mark Girton, MD

Jenna Khan, MD

Nicholas Larkey, PhD

Mani Mahadevan, MD

Melinda Poulter, PhD

Emily Snavely, PhD

Eli Williams, PhD

We open Saturday morning's sessions with the Ellis Benson Award and Lecture, delivered by Dr. Sarah Wheeler of UPMC. After additional morning sessions in laboratory medicine, we close this year's ACLPS meeting.

We would like to thank our many sponsors and other contributors to ACLPS, as well as the ACLPS Program and Finance Committee for wonderful input this past year. We especially want to acknowledge and thank our partners, Custom Management Group, a full-service Association Management Company, without whom ACLPS23 may never have gotten off the ground.

We hope you enjoy your time in Charlottesville, and have the opportunity to explore the biggest little city in Virginia.

Sincerely,

Jim Gorham, Lindsay Bazydlo, and the ACLPS23 Planning Committee

General Information

ACLPS Registration Desk Hours

Lobby, Third Floor

Wednesday, 7 June 2023	4:00 PM-6:00 PM
Thursday, 8 June 2023	7:30 AM-5:00 PM

Rotunda Foyer, Third Floor

Friday, 9 June 2023	7:00 AM-5:00 PM
Saturday, 10 June 2023	7:30 AM-11:20 AM

Special Events

Shuttles to UVA/Downtown Charlottesville; Optional tour of UVA central grounds
Wednesday, 7 June 2023, 4:00–10:00 PM
Shuttles depart from hotel main entrance.

Tour includes the Rotunda, the Lawn (Pavilions, Colonnade Club hotel, gardens, student rooms), Edgar Allen Poe's room, and the Memorial to Enslaved Laborers. *Separate ticket required.*

Downtown Charlottesville features many restaurant options. *Reservations suggested.*

Welcome Reception | Promenade Ballroom
Thursday, 8 June 2023, 6:00–8:00 PM
Networking and heavy hors d'oeuvres

Social Hour and Awards Banquet | Montalto
Friday, 9 June 2023, 6:30–9:00 PM
Shuttles depart from and return to hotel main entrance: 5:20–6:00 PM; 9:00–9:45 PM

Food and Beverage

Only registered attendees may participate in ACLPS food and beverage functions.

Conference registration includes: breakfast; morning and afternoon beverage breaks; lunch; welcome reception; awards banquet.

Name Badges and Dress

You must wear your name badge at all times during the conference to identify yourself as an ACLPS attendee. Remember to remove your badge when leaving the conference venue.

Dress is business casual. We recommend wearing comfortable shoes and dressing in layers that you can add and remove as room temperatures vary throughout the day.

Conference Evaluations

A link to the online evaluations will be emailed to attendees following the conference. Please remember to record your impressions of the conference while you attend.

Continuing Education Credits

Joint Accreditation Statement

JOINTLY ACCREDITED PROVIDER™ INTERPROFESSIONAL CONTINUING EDUCATION

In support of improving patient care, this activity has been planned and implemented by Amedco LLC and Academy of Clinical Laboratory Physicians and Scientists. Amedco LLC is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council forPharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

Physicians

ACCME Credit Designation Statement

Amedco LLC designates this live activity for a maximum of 15.50 *AMA PRA Category 1 Credits™* for physicians. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

For more information on claiming CME credits, visit www.aclps.org/aclps-2023-ce.

Planner and Moderator Disclosures

Carmen Gherasim:	Other (Abbott)
James Gorham:	Research Grant Site Principal Investigator (Cerus)
Ron Jackups:	Consultant (Werfen)
Eric Konnick:	Scientific/Medical Advisory Board Member (Agilent, AstraZeneca, Caris, Roche); Other (Medscape)
Joe Wiencek:	Other (AACC, BioRad, Cardinal Health); Consultant (Cystic Fibrosis Foundation)

No other conflicts were reported by planners or moderators. See pages 16-22 and 26 for speaker disclosures.

About ACLPS

The Academy of Clinical Laboratory Physicians and Scientists (ACLPS) is the leading professional society for academic **Laboratory Medicine** and has active affiliations with **70 academic and community centers** that train residents in clinical pathology. The Academy is driven by the following objectives:

- To encourage and advance the highest standards of education in laboratory medicine in medical school and related curricula.
- To encourage and promote the highest standards of resident training and post-graduate education of physicians and scientists in clinical pathology at universities and medical schools.
- To encourage and promote the highest standards of service, education and research in academic laboratory medicine.

ACLPS members include physicians, scientists, medical technologists with graduate degrees, and educators. We invite all trainees in clinical pathology to consider application for membership. We invite all training programs who are training individuals toward board certification in clinical pathology to encourage their faculty and trainees about the opportunities available through the Academy. Visit www.aclps.org/membership for more information.

Individual Donors | last twelve months

Contributions by the following ACLPS members support the pursuit of excellence in laboratory medicine by helping to fund grants and educational programs.

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Exhibit Table 7

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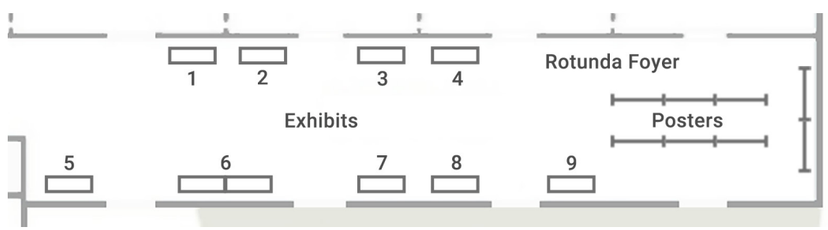

Exhibit Hours

Thursday, 8 June 2023
7:30 am–5:00 pm

Friday, 9 June 2023
7:00 am–5:00 pm

Saturday, 10 June 2023
7:30–11:20 am

Notes

Program Wednesday–Thursday, 7–8 June 2023

Wednesday, 7 June 2023

4:00–6:00 PM	Registration Desk Open | Lobby
4:00–10:00 PM	Shuttles to UVA/Downtown Charlottesville • Optional 30-minute UVA tour (see p. 3) • Downtown restaurants – reservations suggested

Thursday, 8 June 2023

7:30 AM–5:00 PM	Registration Desk Open | Lobby
7:30–8:30 AM	Breakfast | Rotunda Foyer
8:30–10:00 AM	Welcome; Scientific Session 1 | Rotunda Ballroom *Moderator: Lindsay Bazydlo* • Harnessing microfluidics for a small portable, cost-effective system for ultrafast DNA genotyping. James Landers • Immunoglobulin free light chains measurement in CSF as a diagnostic test in multiple sclerosis. Maria Willrich
10:00–10:25 AM	Networking Beverage Break | Rotunda Foyer
10:25–11:50 AM	Scientific Session 2 | Rotunda Ballroom *Moderator: Nick Larkey* • Platelet differentiation. Adam Goldfarb • Building better names for lab tests: The TRUU-Lab initiative. Ila Singh
11:50 AM–1:00 PM	Networking Lunch | Rotunda Foyer
11:50 AM–1:00 PM	Executive Council Lunch | Root 29 Private Room
1:00–2:25 PM	Scientific Session 3 | Rotunda Ballroom *Moderator: Jinbo Fan* • What is metrological traceability and why should you care? Greg Miller • VEXAS syndrome and hematological malignancies: The what, the how, and the why. Ifeyinwa Obiorah
2:25–2:50 PM	Networking Beverage Break | Rotunda Foyer
2:50–5:00 PM	Scientific Session 4 | Rotunda Ballroom *Moderator: Eli Williams* • Health is wealth: Designing equitable clinical laboratories for thriving communities. Octavia Peck-Palmer • Chimeric RNA fusions and their implications in cancer. Li Hui • A winning formula for a medical laboratory formulary. Jim Harrison
6:00–8:30 PM	Welcome Reception | Promenade Ballroom & Patio


James Landers, PhD (UVA)


Maria Willrich, PhD (Mayo Clinic)
Disclosures: Page 22


Adam Goldfarb, MD (UVA)


Ila Singh, MD, PhD (Baylor)


W. Greg Miller, PhD (VCU)


Ifeyinwa Obiorah, MD, PhD (UVA)


Octavia Peck-Palmer, PhD (Pittsburgh)
Disclosures: Page 20


Hui Li, PhD (UVA)


Jim Harrison, MD, PhD (UVA)

Speaker Biographies: Pages 16-22

Program Friday, 9 June 2023

7:00 AM–5:00 PM Registration Desk Open | Rotunda Foyer

7:00–8:00 AM Breakfast | Rotunda Foyer

8:00–9:30 AM Young Investigator Abstract Presentation Breakouts A | Abstract pages 27-48

A1 Coagulation | Montdomaine
8:00–9:15 AM

Moderators: Lindsay Bazydlo, Delores Mo

A1-1 Performance of a direct oral anticoagulant removal reagent, DOAC-Stop™ for lupus anticoagulant testing. Mark Girton (UVA)

A1-2 Quality analysis of lupus anticoagulant testing: Indeterminate and interference. Timothy Bell (Cleveland Clinic)

A1-3 Using an agonist panel and aggregation to assess antiplatelet therapy in mice. Dominique Gordy (Columbia)

A1-4 Use of plasmapheresis in heparin induced thrombocytopenia in patients undergoing urgent cardiac surgery. Ejas Palathingal Bava (Henry Ford Hospital)

A1-5 Anticoagulation management in patients tested for heparin-induced thrombocytopenia in the cardiothoracic intensive care unit diverges from expert guidelines. Nicholas Spies (Wash U)

A2 Toxicology | Albemarle
8:00–9:00 AM

Moderators: Carmen Gherasim, Brian Kelly

A2-1 Phosphatidylethanol as a biomarker to assess alcohol exposure in women of reproductive age using retrospective data from a reference laboratory. Nicole Mathewson (Utah)

A2-2 Lorazepam detection with urine benzodiazepines screening tests: Not all tests are created equal. Tanjina Akter (MUSC)

A2-3 Evaluation of siltuximab and tocilizumab analytical interference on interleukin 6 measurements. Qian Wang (Mayo Clinic)

A2-4 Take precaution with choice of pastry: Poppy seed-containing products cause significantly positive results in urine drug tests. Rebecca Wilson (UW)

A3 Microbiology | Gallery B
8:15–9:30 AM

Moderators: Emily Snavely, Arthur Totten

A3-1 Enteric pathogens within the men who have sex with men population, associated risk factors, and provider vigilance: Analyzing three years of BioFire® data with retrospective chart review. Timothy Miller (UW)

A3-2 Multilocus sequence typing of emerging azole-resistant candida auris isolates from critically ill patients in a New York City medical center. Maxwell Weidmann (Columbia)

A3-3 Evaluation of clinically tractable methods for treponema pallidum DNA extraction from whole blood. Joshua Lieberman (UW)

A3-4 Antimicrobial susceptibility patterns among a large, nationwide cohort of chryseobacterium species clinical isolates. Jonathan Pham (Utah)

A3-5 Evaluation of the LifeScale system for rapid phenotypic antimicrobial susceptibility testing from positive blood cultures. Daniel Montelongo-Jauregui (Utah/ARUP)

10:00–10:25 AM Networking Beverage Break | Rotunda Foyer
Poster Presentations (see pp. 14-15) | Rotunda Foyer

Continued on page 10

Notes

A4 Immunology | Gallery A
8:15–9:15 AM

Moderators: Jim Harrison, Joe Wiencek

A4-1 An unbiased approach of individual tissue-specific autoantibody identification using immunoprecipitation coupled to mass spectrometry (IP-MS). Friederike Antonia Arlt (Universitätsmedizin Berlin)

A4-2 Evaluation of different microbead volumes in a single antigen bead assay for HLA antibody detection. Robert Frick (Wash U)

A4-3 Enhanced IgG immune response to COVID-19 vaccination in sickle cell disease compared to general outpatient population. Hirotomo Nakahara (Emory)

A4-4 Observations from Mass-Fix: Prevalence and characteristics of therapeutic monoclonal antibodies (t-mabs) detected by isotyping of monoclonal immunoglobulins via MALDI-TOF mass spectrometry. Ria Fyffe-Freil (Mayo Clinic)

A5 Hemoglobin and Troponin Testing | Gallery C
8:30–9:30 AM

Moderators: Nick Larkey, Adina Badea

A5-1 Impact of implementing point of care hemoglobin A1C testing in an obstetrics outpatient clinic. Homayemem Weli (Wash U)

A5-2 Resolving the impact of hs-Troponin I carryover on Beckman Coulter Access DXI 800 in academic hospital sttings. Xu Li (Emory)

A5-3 Comparability of Beckman Coulter Access Cardiac Troponin I Assays. Caroline Stanek (Alabama)

A5-4 Hemoglobin A1c control is an independent predictor of circulating troponin concentrations using machine learning. Hannah Brown (Wash U)

Abstract Session A Speaker Disclosures

No conflicts

Program Friday, 9 June 2023 | continued

10:30 AM–12:00 PM Young Investigator Abstract Presentation Breakouts B | Abstract Pages 49-74

B1 Young Investigator Award with Distinction | Gallery C
10:30 AM–12:00 PM
Moderators: Josh Lieberam, John Luckey

- B1-1 Development of a machine learning decision support system for clinical flow cytometry. Joseph Lownik (Cedars-Sinai)
- B1-2 Automated machine learning-based diagnosis and molecular characterization of acute leukemias using flow cytometry data. Joshua Lewis (Harvard)
- B1-3 POT1b represses ATR DNA damage response at telomeres. Taylor Takasugi (Yale)
- B1-4 Role of T cell immunosenescense in modulating gut microbiome. Sithara Vivek (UMinn)
- B1-5 Comparison of two free light chain assays: Performance of the free light chain ratio as risk factor for MGUS progression. Benjamin Andress (Mayo Clinic)
- B1-6 Identification of extracellular vesicle-based protein markers of disease pathology in Alzheimer's disease. Patrick Vanderboom (Mayo Clinic)

B2 Chemistry | Gallery B
10:30–11:45 AM
Moderators: Kayode Balogun, Anna Merrill

- B2-1 LC/MS-MS quantification of myo-inositol: A novel biomarker for kidney disease. Catherine Omosule (Wash U)
- B2-2 Alternative strategies to provide actionable results when supply of urinalysis strips is unavailable. Jeannette Guarner (Emory)
- B2-3 Assessing the reliability of creatinine-estimated glomerular filtration rate in living kidney donor candidates: Does it measure up to the measured rate? Sarrah Lahorewala (Houston Methodist)
- B2-4 Analytical performance evaluation of BioRad's Unassayed Multiqual, Immunoassay Plus and Assayed Multiqual InteliQ tube-based quality control materials. Erving Laryea (Vanderbilt)
- B2-5 Rapid resolution of medically relevant polyunsaturated, very long-, odd-, and branched-chain fatty acid methyl esters. Andrew Nelson (Texas)

B3 Informatics and Lab Management | Gallery A
10:30 AM–11:45 PM
Moderators: Ron Jackups, Patrick Mathias

- B3-1 Creating a reference interval database to support clinical AI/ML applications with generalizable laboratory phenotypes. Thomas Durant (Yale)
- B3-2 Evaluating the utility and challenges associated with "anonymous" patients in the electronic medical record. Kai Rogers (Iowa)
- B3-3 Recycling opportunities in a high volume academic clinical chemistry laboratory. Raeshun Glover (Vanderbilt)
- B3-4 Analysis of daratumumab reporting in type and screen orders to identify opportunities for information system improvement. Patrick Morse (Wash U)
- B3-5 PathBrowser: An educational tool to convert textbook images and captions into flashcards. Stevephen Hung (GW)

11:50 AM – 1:00 PM Lunch | Rotunda Foyer
ACLPS Business Meeting | Rotunda Ballroom

Continued on page 12

Notes

B4 Transfusion Medicine | Montdomaine
10:30 AM–12:00 PM
Moderators: Jenna Khan, Valery Kogler

- B4-1 Trends in hematopoietic stem cell utilization and cost of cryopreservation. Travis Jebackumar (Baylor)
- B4-2 A stochastic multicompartment model of hemostasis and oxygenation during trauma resuscitation as a platform for in silico trials of transfusion. Casey Vieni (NYU)
- B4-3 Residual component culture: Application of standardized transfusion reaction culture criteria to reduce culture rates. Kyle Hodge (UVA)
- B4-4 Did interventions in a massive transfusion protocol program change transfusion practice? Ronald Devera (UVA)
- B4-5 Developing a flow cytometry-based approach to measure post-transfusion RBC survival. Anabel Miller (Columbia)
- B4-6 Preoperative determination of red blood cell transfusion for orthotopic liver transplantation in the age of artificial intelligence. Mohammad Barouqa (Cleveland Clinic)

B5 Molecular | Albemarle
10:45 AM–12:00 PM
Moderators: Eric Konnick, Hui Li

- B5-1 Simplifying molecular testing through electronic order entry. Regina Kwon (UW)
- B5-2 Strategies for validation of a low-volume BCR:ABL p190 assay in the clinical laboratory. Patricia Hernandez (Wash U)
- B5-3 Optimized method to enhance the limit of detection for large FLT3 internal tandem duplications. Zita Hubler (Wash U)
- B5-4 Caffeine, Lorazepam, and Morphine use in neonatal intensive care unit population and potential relevance of pharmacogenomics. Seyi Falekun (Utah/ARUP)
- B5-5 Tissue fixation significantly impacts MLH1 promoter methylation analysis: A quality improvement study. Yongsang Park (UVA)

Abstract Session B Speaker Disclosures
Thomas Durant: Consultant (Abbott, Roche)

Program Friday, 9 June 2023 | continued

1:30–2:30 PM

Ernest Cotlove Lecture & Award | Rotunda Ballroom

Moderator: Melinda Poulter

- The "next" pandemic — antibacterial resistance. Amy Mathers

Amy Mathers is an Associate Professor of Medicine and Pathology at the University of Virginia. She is the Clinical Director of the Adult Antimicrobial Stewardship Program, Director of the Microbiology Genomic Sequencing Clinical Laboratory and Associate Director of Clinical Microbiology for the University of Virginia. She is Vice Chair of the Clinical and Laboratory Standards Institute Antimicrobial Susceptibility Testing Subcommittee.

She has focused her clinical and research efforts on the urgent clinical problem of laboratory detection and hospital transmission of antimicrobial resistant bacteria. Molecular characterization has included analysis of mobile resistance mechanisms with evaluation of plasmid evolution and mobility across species with next generation sequencing paired with more traditional techniques. Her current research also involves development of molecular techniques for detection and tracking of antimicrobial resistance for public health surveillance and response.

2:25–2:50 PM

Networking Beverage Break | Rotunda Foyer

Poster Presentations (see pp. 10-11) | Rotunda Foyer

3:00–5:10 PM

Scientific Session 5 | Rotunda Ballroom

Moderator: Emily Snavely

- Digital imaging and machine learning for stool parasite detection. Marc Couturier
- Toward antiracist medicine. Greg Townsend

Strandjord Young Investigator Grant Presentations

- Characterizing the clonal structure of primary and secondary B cell responses in the murine KEL alloimmunization model. Edward Lee
- Ultrasensitive and minimally invasive diagnostic assay for targeting the oncogenic transcription factor SALL4: Development and validation. Jun Liu
- IgG glycosylation of anti-dsDNA autoantibodies as a novel biomarker for systemic lupus erythematosus. Rebecca Treger

5:20–6:00 PM

Shuttles to Montalto | Hotel Main Entrance

6:30–9:00 PM

Social Hour and Awards Banquet | Montalto

9:00–9:45 PM

Shuttles return to DoubleTree hotel

Amy Mathers, MD (UVA)
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Marc Couturier, PhD, D(ABMM) (Utah)
Disclosures: Page 16

Gregory Townsend, MD (UVA)

Edward Lee, MD, PhD (Yale)

Jun Liu, MD, PhD (Harvard)

Rebecca Treger, MD, PhD (UW)

Speaker Biographies: Pages 16-22

Awards Information: Pages 23-25

Program Saturday, 10 June 2023

7:30–11:20 AM

Registration Desk Open | Rotunda Foyer

7:30–8:30 AM

Breakfast | Rotunda Foyer

8:30–9:30 AM

Ellis Benson Lecture & Award | Rotunda Ballroom

Moderator: Chris Tormey

- Using data to improve laboratory medicine for special populations. Sarah Wheeler

Dr. Sarah Wheeler is an Associate Professor at the University of Pittsburgh, Department of Pathology, Medical Director of Clinical Chemistry at UPMC Children's Hospital of Pittsburgh, Medical Director of the Automated Testing Laboratory at UPMC Mercy Hospital, and Associate Medical Director of Clinical Immunopathology at UPMC. Her research interests include infectious disease serology screening assays (SARS CoV2, HIV, syphilis, lyme, hepatitis), rapid point of care diagnostics, effects of viral infections on autoimmunity, machine learning to improve diagnosis, and appropriate serology testing in children with immune dysregulation.

9:30–9:45 AM

Networking Beverage Break | Rotunda Foyer

9:45–11:10 AM

Scientific Session 6 | Rotunda Ballroom

Moderator: Mark Girton

- High-throughput metabolomics: Towards personalized transfusion medicine. Angelo D'Alessandro
- Variants of patient IgG genes alter results of laboratory testing. Jim Zimring

11:10–11:20 AM

Closing Remarks

11:50 AM–1:00 PM

Executive Council Lunch | Root 29 Private Room

Sarah Wheeler, PhD (Pittsburgh)
Disclosures: Page 22

Angelo D'Alessandro, MD (Colorado)
Disclosures: Page 16

Jim Zimring, MD, PhD (UVA)

Speaker Biographies: Pages 16-22

Awards Information: Pages 23-25

Posters

Abstracts: Pages 75-88

P01 Retrospective evaluation of Mycoplasma genitalium prevalence and macrolide resistance in a study cohort of pregnant women in central Alabama from 1997-2001. Arthur Totten (Stony Brook)

P02 Prevalence of Bacteremia Due to Streptococcus/Enterococcus Species at an Academic/ Community Health System Over a Five Year Period. Christopher Zarbock (UMinn)

P03 In vitro analysis of potential drug loss of tacrolimus and modified cyclosporine via nasogastric tube. Yi Xiao (Children's Hospital, LA)

P04 Comparing refrigeration to immediate room temperature testing for uric acid monitoring in rasburicase-treated patient. Brittany Young (Utah)

P05 Point-of-care HIV testing send outs integration in laboratory LIS using the NOVA StatStrip glucometer. Mari Ishak Gabra (Children's Hospital, LA)

P06 Performance of a modified ALLType NGS HLA Typing Assay with the Ion Chef/Ion S5/TypeStream visual system. Manli Shen (Wash U)

P07 Utility of blood culture bacterial phenotype confirmation of rapid molecular identification: A case report. Paul Bernard (Yale)

P08 Caffeine, lorazepam, and morphine use in neonatal intensive care unit population and potential relevance of pharmacogenomics. Seyi Falekun (Utah)

P09 Evaluating the performance of ChatGPT in writing autopsy clinicopathological correlations. Matt Andrew Paz (UMinn)

P10 Utility of Vizient Clinical Data Base as a benchmarking tool for laboratory stewardship programs. Subhashree Mallika Krishnan (UMich)

P11 Characterization of PIK3CA mutation testing in metastatic breast adenocarcinomas: a multi-site, single institution study. Jim Hsu (Houston Methodist)

P12 Discordant indirect immunofluorescence compared to multiplex bead immunoassay in ANCA associated vasculitides, a retrospective analysis. Subhashree Mallika Krishnan (UMich)

P13 Change in HbA1c post-transfusion is correlated to pre-transfusion HbA1c result. Grace Kroner (Cleveland Clinic)

P14 Evaluating the effectiveness of pseudothrombocytopenia (PTCP) panel with alternative anticoagulants on clinically suspicious EDTA-dependent PTCP: A single tertiary hospital experience. Fahad Sheikh (Albert Einstein)

Continued, next page

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Posters | continued

Abstracts: Pages 89-100

P15 Development and validation of a liquid chromatography mass spectrometry method to measure highly concentrated tacrolimus and cyclosporine specimens prepared from commercial pharmaceutical products to assess administration through feeding tubes. Yi Xiao (Children's Hospital, LA)

P16 A rare case of compound Hemoglobin Lansing/Hemoglobin S coinherited with alpha thalassemia trait (-alpha3.7) presented with spurious hypoxemia and moderate hemolytic anemia. Adwait Marhatta (Albert Einstein)

P17 *Withdrawn*

P18 Comparison of blood tubes for chemistry analytes across three manufacturers. Tatiana Coverdell (NIH)

P19 An organization-wide analysis of laboratory test cost variables and costs as displayed in the electronic health record: first steps. Karen Fang (UW)

P20 Improved test utilization after implementation of a high-sensitivity cardiac troponin I: Real-world experience in a U.S. emergency department of an academic urban hospital. Laura Warren (Cornell)

P21 Impact of CMA on diagnosis and clinical management of neonates: A retrospective single center study of a 10-year cohort. Ozgur Rosti (UVA)

P22 Platelet inhibition testing: Whole blood point-of-care vs traditional platelet aggregometry. Robert Achram (Emory)

P23 Bone marrow differential cell count uncertainty in the classification of plasma cell neoplasms. Conrad Shebelut (Emory)

P24 The Million Patient Labset: A large, de-identified dataset of longitudinal clinical laboratory results from one million patients. Nicholas Spies (Wash U)

P25 Delayed hemolytic transfusion reactions could be prevented by a national alloimmunization registry. Caroline Stanek (UAB)

P26 Monitoring infected reticulocytes during murine malaria infection. Dominique Gordy (Columbia)

Notes

Invited Speaker Biographies and Disclosures

Marc Couturier, PhD, D(ABMM)

University of Utah

Dr. Couturier is a professor of pathology at the University of Utah School of Medicine and a medical director at ARUP Laboratories, serving as director of parasitology, antigen testing, and emerging public health crises. He received his PhD in medical microbiology and immunology with a specialty in bacteriology from the University of Alberta in Edmonton, Alberta, Canada. Dr. Couturier served as a research associate at the Alberta Provincial Laboratory for Public Health and completed a medical microbiology fellowship at the University of Utah. His clinical research interests include improved diagnostics for emerging agents of infectious gastroenteritis and improving/modernizing diagnostic parasitology testing. Marc is the Clinical microbiology fellowship director at the University of Utah. Dr. Couturier is board certified in medical microbiology through the American Board of Medical Microbiology, and a member of the American Society for Microbiology, American Society for Clinical Pathology, and Academy of Clinical Laboratory Physicians and Scientists, and a member of the College of American Pathologists microbiology resource committee where he serves as the parasitology lead. Dr. Couturier has authored over 70 publications and numerous textbooks and chapters. In his free time, Dr. Couturier coaches competitive junior hockey teams in Utah.

Disclosures: Consultant (bioMerieux);
Private Stock Shareholder (bioMerieux);
Scientific/Medical Advisory Board Member (Seegene);
Speakers Bureau (Genetic Signatures);
Other (bioMerieux, Techcyte)

Angelo D'Alessandro, MD

University of Colorado

Dr Angelo D'Alessandro is a tenured Full Professor in the Department of Biochemistry and Molecular Genetics, with other appointments in Surgery and Medicine – Division of Hematology. He is the founder and Director of the Metabolomics Core of CU Anschutz School of Medicine; the director of the Mass Spectrometry Shared Resource for the University of Colorado Cancer Center; the director for the Metabolomics Core for the Trauma Research Center, the Pulmonology Center, the Lidna Crnic Institute for Down Syndrome. Despite the young age (38), he has published over 415 papers, research sponsored by NHLBI and NIGMS. He is founder and CSO of Omix Technologies Inc, Altis Biosciences, and serves as an advisory board member forHemanext Inc, Forma Therapeutics Inc, and Macopharma. He is a Boettcher Investigator, National Blood Foundation Scholar, and recipient of the Jean Julliard Award (ISBT), Innovation Award and RISE Award in Transfusion Medicine (AABB). He is an affiliate investigator to the Vitalant Research Institute, the Linda Crnic Institute for Down syndrome, the Gates Grubstake Center for Regenerative Medicine.

Disclosures: Scientific/Medical Advisory Board Member (Hemanext Inc, Macopharma Inc)

Invited Speaker Biographies and Disclosures

Adam Goldfarb, MD

University of Virginia

Adam Goldfarb is a Professor of Pathology at University of Virginia School of Medicine, where he has been for the past 25 years. During this time, he has combined a clinical practice in Hematopathology with an extramurally funded research program. The research has focused on the developmental biology of red cells and platelet-producing cells. He has served as chief of the Experimental Pathology Division for the past decade and has served on the executive committee of the University of Virginia Medical Scientist Training Program for the past 7 years. At a national level, he has served on more than 50 peer review panels including the Leukemia Immunology and Blood Cells Group at the American Cancer Society and a recent appointment as a standing member to the DDK-G panel at the NIDDK/NIH.

Disclosures: No Conflicts

Jim Harrison, MD, PhD

University of Virginia

James Harrison, MD, PhD, is Professor of Pathology, Director of Clinical Laboratory Informatics, Associate Director of Clinical Chemistry, and the Quality and Patient Safety Officer in the Department of Pathology at the University of Virginia. He also co-chairs the Clinical Laboratory Stewardship Subcommittee in the UVA Health System. His work in informatics has included formal roles in the installation and management of clinical laboratory information systems, electronic health records, clinical decision support, institutional clinical trials management systems, biorepository systems, and institutional clinical data repositories, and he is active in resident training, clinical analytics, and software development. He has received funding as PI for R-01 and T-15 grants in informatics from the NLM and NCI. He is chair of the College of American Pathlogists (CAP) Informatics Committee and a member of the CAP Council on Informatics and Pathology Innovation, the CAP Artificial Intelligence Committee, and the CAP Information Technology Leadership Committee. He serves as a CAP liaison to the Pathology and Laboratory Medicine Workgroup of the Integrating the Healthcare Enterprise standards organization and the Pathology Informatics Essentials for Residents (PIER) Steering Committee.

Disclosures: No Conflicts

James Landers, PhD

University of Virginia

James Landers is a Jefferson Scholars Faculty Fellow and Commonwealth Professor of Chemistry, Professor of Mechanical Engineering, and an Associate Professor of Pathology at the University of Virginia. He holds both bachelor and PhD degrees in Biochemistry from the University of Guelph (Canada), with post-doctoral fellowships at the Hospital for Sick Children in Toronto, the University of Toronto School of Medicine and the Mayo Clinic. His research program focuses on the development of fully-integrated microfluidic systems for sample-to-result genetic analysis. He has published more than 275 papers, 25 book chapters, founded three start-up companies, and serves as the CoEditor-in-Chief for the journal *Analytica Chimica Acta*.

Disclosures: None Reported

Invited Speaker Biographies and Disclosures

Edward Lee, MD, PhD | 2022 Paul Strandjord Young Investigator Grant

Yale University

Edward Lee is a clinical pathology resident in the Department of Laboratory Medicine at Yale University School of Medicine and will be a transfusion medicine fellow at Yale in the upcoming academic year. He is also in the research track and currently performing research with Steven Kleinstein. He received his PhD from the University of Glasgow and received his MD from Albert Einstein College of Medicine. His current research interests include developing computational tools for analyzing adaptive immune receptor repertoire sequencing (AIRR-seq) and single-cell RNA sequencing data and leveraging these techniques to understand the immunology of RBC alloimmunization.

Disclosures: No Conflicts

Hui Li, PhD

University of Virginia

Dr. Hui Li is a tenured Full Professor in the Department of Pathology, and the Department of Biochemistry and Molecular Genetics, at the University of Virginia. He is also the Harrison Distinguished Teaching Professor, and currently serves as the program co-director of the Cancer Center. Since its establishment 13 years ago, his lab has focused on gene fusion, chimeric RNA, and other cancer genetics related topics. His lab has been funded by NCI, NIGMS, Stand Up to Cancer, American Cancer Society, V Foundation, St. Baldrick Foundation, and other foundations. The Li lab has been working on various cancer types, including prostate, colon, cervical, bladder, glioma, sarcoma, etc. His lab's research has resulted in publications at journals including *Science*, *Cancer Discovery*, *PNAS*, and *Nature Communications*, and in several patents. His lab has trained 9 PhD candidates, 10 postdoctoral fellows, 16 visiting scholars, and 45 undergraduates.

Disclosures: No Conflicts

Jun Liu, MD, PhD | 2022 Paul Strandjord Young Investigator Grant

Harvard University

Hailing from Nanjing, China, Jun holds a PhD in developmental biology from University of Cambridge, UK, and MD from Harvard Medical School. During her time as a clinical pathology resident at Brigham and Women's hospital, Jun has been working as a post-doctoral fellow under the guidance of Dr. Li Chai and collaborating with other renowned mentors in the hematology/oncology and transfusion medicine fields such as Dr. Daniel Tenen and Dr. William Lane. Jun's research work includes developing novel therapies for hemoglobinopathies, therapeutic targeting of oncogenic transcription factor SALL4, and developing SALL4-centered biomarker assays in myeloid malignancies and solid tumors. Her work on this latter project earned her team the honor of being one of the three finalists for the Brigham BRight Future Prize research competition in 2022. Passionate about biotech and research translation, Jun co-led a team that helped shepherd the SALL4 targeted degradation and companion diagnostics project to the thriving biotech scene of Boston. The project was selected as a finalist for the Boston Nucleate Activator Program cohort 2023, and won the "Tough Tech Prize" in the annual Harvard Business School New Venture Competition in 2023. Jun loves hiking, traveling, (blind) wine tasting, and doing yoga with her toddlers. She

Invited Speaker Biographies and Disclosures

is thrilled to start her fellowship in transfusion medicine at the Harvard Combined Transfusion Medicine program in July 2023.

Disclosures: No Conflicts

Amy Mathers, MD | 2023 Ernest Cotlove Award

University of Virginia

Amy Mathers is an Associate Professor of Medicine and Pathology at the University of Virginia. She is the Clinical Director of the Adult Antimicrobial Stewardship Program, Director of the Microbiology Genomic Sequencing Clinical Laboratory and Associate Director of Clinical Microbiology for the University of Virginia. She is Vice Chair of the Clinical and Laboratory Standards Institute Antimicrobial Susceptibility Testing Subcommittee.

She has focused her clinical and research efforts on urgent clinical problem of laboratory detection and hospital transmission of antimicrobial resistant bacteria. Molecular characterization has included analysis of mobile resistance mechanisms with evaluation of plasmid evolution and mobility across species with next generation sequencing paired with more traditional techniques. Her current research also involves development of molecular techniques for detection an tracking of antimicrobial resistance for public health surveillance and response.

Disclosures: Scientific/Medical Advisory Board Member (Cepheid, DayZeroDiagnostics, Merck, OpGen, QPex, VenatoRx)

W. Greg Miller, PhD

Virginia Commonwealth University

Greg Miller is a Professor in the Pathology Department at Virginia Commonwealth University where he serves as Co-Director of Clinical Chemistry and Director of Pathology Information Systems. He is an active contributor to several committees and working groups for standardization and harmonization of laboratory results, and external quality assessment/ proficiency testing. He currently chairs the Joint Committee for Traceability in Laboratory Medicine and the IFCC working group for commutability in metrological traceability. He is a past-president of the American Association for Clinical Chemistry and of the Clinical and Laboratory Standards Institute.

Disclosures: No Conflicts

Ifeyinwa Obiorah, MD, PhD

University of Virginia

Ifeyinwa (Ifey) Obiorah, is an Assistant Professor of Pathology at University of Virginia Health and a diagnostician on the Hematopathology Service. She obtained her medical degree from Nnamdi Azikiwe University, Nigeria and received a PhD degree in Tumor Biology from Georgetown University, Washington DC where she worked on the modulation of estrogen-induced apoptosis in breast cancer. Dr Obiorah subsequently completed her residency training in Anatomic and Clinical Pathology at the Georgetown University Hospital, where she served as Chief Resident. She went on to complete her fellowship training in Hematopathology at the National

Invited Speaker Biographies and Disclosures

Institute of Health, Bethesda. Dr. Obiorah's clinical research focuses on diagnostics in hematological malignancies and has worked on several projects including VEXAS syndromes, germline predisposition to myeloid neoplasms and molecular characterization of cutaneous lymphomas. She has authored over 30 publications and also serves as a strategist in improving diversity, equity and inclusion in pathology.

Disclosures: No Conflicts

Octavia Peck-Palmer, PhD

University of Pittsburgh

Octavia M. Peck Palmer earned her PhD in Physiology from The Medical University of South Carolina, in Charleston, SC. She then completed a postdoctoral fellowship in clinical chemistry at Washington University School of Medicine in Saint Louis, MO.

She is a board-certified clinical chemist and Associate Professor in the Department of Pathology at the University of Pittsburgh School of Medicine, in Pittsburgh, PA. She has secondary faculty appointments in the departments of Critical Care Medicine and Clinical and Translational Science. Since 2017, she has served as the Division Director of Clinical Chemistry at the University of Pittsburgh Medical Center (UPMC). She is the Medical Director of several CAP/CLIA-accredited clinical laboratories (automation, point-of-care testing, and STAT) within UPMC's healthcare system, since 2008. She also teaches (i.e., Race in Medicine course) and mentors undergraduates, graduates, residents, fellows, medical technologists and junior faculty.

Dr. Peck Palmer is a NIH-funded translational researcher, and her research interests include clinical and translational studies of sepsis, laboratory quality assurance, clinical test development, and recognizing laboratory medicine's role in eliminating health disparities. She is also the faculty director of the Clinical Research and Biospecimen Core Laboratory within the Clinical Research, Investigation, and Systems Modeling of Acute Illness (CRISMA) Center in the Department of Critical Care Medicine at the University of Pittsburgh School of Medicine. She is the chair of the Clinical and Laboratory Standards Institute document writing group for the Clinical Testing for Early Detection and Management of Sepsis, 1st Edition.

Notably, Dr. Peck Palmer is President-Elect of the American Association of Clinical Chemistry (AACC) (term commencing 1 August 2023). An active member of AACC since 2006, she is chair of the AACC Health Equity and Access Division, which she founded, and past chair of the AACC Diversity, Equity, and Inclusion governance committee.

Disclosures: Consultant (Abbott, Cytovale, Roche Diagnostics, Werfen);
Research Grant Site Principal Investigator (Siemens Healthineers);
Scientific/Medical Advisory Board Member (Siemens Healthineers)

Ila Singh, MD, PhD

Baylor University

Ila Singh, M.D, PhD serves as Chief of Laboratory Medicine, and Chief of Pathology Informatics at Texas Children's Hospital. She is a Professor of Pathology & Immunology at Baylor College of Medicine. Ila is the founding director of the Clinical Informatics fellowship program at Baylor College of Medicine. She has special expertise in Laboratory Test Utilization Stewardship. Her current research is focused on using Machine Learning approaches to determine risk stratification, prescriptive analytics, better utilization of healthcare resources, and optimization of treatment protocols. She

Invited Speaker Biographies and Disclosures

is the founder of TRUU-Lab, a national initiative to change the names of clinical lab tests to those that are more standardized and easily understood by clinicians.

Ila completed her MD at the University of Bombay, and her PhD at Yale University. She served as a Jane Coffin Childs Fellow at Stanford University and completed her Clinical Pathology residency training at Columbia University Medical Center in New York City. Ila is dual board-certified in Clinical Pathology and in Clinical Informatics.

Disclosures: No Conflicts

Gregory Townsend, MD

University of Virginia

Dr. Townsend, a native of upstate New York, earned his bachelor's degree at the College of William and Mary, and received his MD from the University of Virginia School of Medicine. After completing a combined residency in internal medicine and pediatrics at West Virginia University, he returned to UVA for a fellowship in infectious diseases, and has been at the University since then. At the time he joined the faculty, he was one of a handful of African-American faculty members in the School of Medicine. He is currently Associate Professor of Medicine in the Division of Infectious Diseases and International Health, Department of Medicine.

Dr. Townsend's primary clinical focus is the care and treatment of individuals with HIV. He is Associate Director of the UVA Infectious Diseases Clinic and Director of its Ryan White program, and principal investigator on several federally funded grants aimed at providing better care for patients living with HIV-AIDS. He has won numerous awards as a clinician and educator, and was an inaugural member of UVA School of Medicine's Academy of Distinguished Educators.

Dr. Townsend's interest in diversity has been shaped by his personal experience as an underrepresented minority in academic medicine, and by his clinical interest in the treatment of HIV — a disease that has a disproportionate impact on racial minorities, the poor, and otherwise disenfranchised members of society. He has been a member of the School of Medicine's Diversity Consortium since its inception. Dr. Townsend shares general responsibility for promoting the educational mission of the School and provides leadership, information, and counsel to students, faculty, and staff to facilitate a positive experience for all as part of a diverse, equitable and inclusive community.

Disclosures: No Conflicts

Rebecca Tregar, MD, PhD | 2022 Paul Strandjord Young Investigator Grant

University of Washington

Dr. Treger earned her MD and PhD degrees from Yale University, where she carried out research investigating innate and adaptive immunity to endogenous retroviruses. She is currently completing her clinical pathology training at the University of Washington, where she has focused on quality improvement and method development projects in Clinical Immunology. Following residency, Dr. Treger will join the Department of Laboratory Medicine & Pathology at the University of Washington as an Assistant Professor. Her long-term career goal is to improve and develop new methods for autoantibody testing in the clinical laboratory.

Disclosures: No Conflicts

Invited Speaker Biographies and Disclosures

Sarah Wheeler, PhD | 2023 Ellis Benson Award

University of Pittsburgh

Dr. Sarah Wheeler is an Associate Professor at the University of Pittsburgh, Department of Pathology, Medical Director of Clinical Chemistry at UPMC Children's Hospital of Pittsburgh, Medical Director of the Automated Testing Laboratory at UPMC Mercy Hospital, and Associate Medical Director of Clinical Immunopathology at UPMC. Her research interests include infectious disease serology screening assays (SARS CoV2, HIV, syphilis, lyme, hepatitis), rapid point of care diagnostics, effects of viral infections on autoimmunity, machine learning to improve diagnosis, and appropriate serology testing in children with immune dysregulation.

Disclosures: Consultant (Abbott, Sebia);
Research Grant Overall Principal Investigator (Siemens Healthineers)

Maria Willrich, PhD

Mayo Clinic

Dr. Maria Alice V. Willrich received her PhD degree from the School of Pharmaceutical Sciences of the University of Sao Paulo, Sao Paulo, Brazil, followed by a clinical chemistry post-doctoral fellowship at Mayo Clinic, in Rochester, MN. She holds the academic rank of Associate Professor of Laboratory Medicine and Pathology, Mayo Clinic College of Medicine, and is a co-director in the Protein and Antibody Immunology Laboratories and the Clinical Mass Spectrometry Laboratory, as well as program director of the post-doctoral clinical chemistry fellowship program in the Department of Laboratory Medicine and Pathology at Mayo Clinic. Her research projects span four areas related to protein testing and immunology: laboratory testing for the monoclonal gammopathies, analysis of immunoglobulins free light chains in serum and in cerebrospinal fluid, the complement system and development of methods of detection for monoclonal antibody therapeutics using mass spectrometry.

Disclosures: Scientific/Medical Advisory Board Member (Myeloma 360);
Research Grant Site Principal Investigator (Sebia Inc., Siemens)

Jim Zimring, MD, PhD

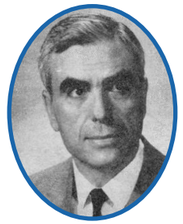
University of Virginia

Dr. James C. Zimring has a PhD in Immunology and an MD, both from Emory University. He is board certified in Clinical Pathology, a diplomate of the American Board of Pathology, and an elected member of the American Society of Clinical Investigation. Dr. Zimring has served as a consultant for the FDA, the Department of Defense, as a frequent grant reviewer for the N.I.H., and is on the scientific advisory board for Canadian Blood Services. He has also served on the Board of Directors for the AABB (Association for the Advancement of Blood and Biotherapies). Dr. Zimring has previously held professorships at Emory University and the University of Washington, and has served as Director of the Puget Sound Blood Center Research Institute and Chief Scientific Officer for the Puget Sound Blood Center. Currently, Dr. Zimring holds the Thomas W. Tillack Chair in Experimental Pathology at the University of Virginia. He has maintained an N.I.H. funded laboratory for over 20 years, has published 180 research articles, and pursues research in diseases of the blood and in diagnostic approaches to serology-based laboratory medicine.

Disclosures: No Conflicts

Awards

Ernest Cotlove Lectureship



Dr. Cotlove was one of the most enthusiastic and active organizers of ACLPS from our beginning. His absorbing interests and work helped mold our purpose and philosophy: progressive education in laboratory medicine and applied clinical research. Ernie, as he was affectionately known to his colleagues, was unshakably committed to the best possible patient care as a first priority. To him this meant thorough grounding in laboratory medicine and the highest attainable precision and accuracy in testing procedures and interpretation. Another characteristic was Ernie's genuine pleasure in mastering areas of new knowledge whether they be biochemistry, physiology, electronics, or golf. Thus, he was a stimulating and thorough teacher of residents, fellows, and attending physicians.

Ernest Cotlove's scientific and medical career started at NYU where, after finishing medicine in 1943, he pursued studies in renal physiology and chemistry. His outstanding ability to acquire knowledge and conduct innovative investigations earned him an invitation from James Shannon, then Director of the National Heart Institute at NIH. He continued studies of renal physiology and chemistry until 1953 when he became Head of Clinical Chemistry Laboratories in the new Department of Clinical Pathology being developed by George Z. Williams during the Clinical Center's construction. Dr. Cotlove seized the opportunity to design and equip the most advanced and functional clinical chemistry facility in our country.

Dr. Cotlove's career exemplified the progress seen in medical research and technology. He designed the electronic chloridometer that bears his name, in spite of published reports that such an approach was theoretically impossible.

He used this innovative skill to develop new instruments and methods at the Clinical Center. Many recognized him as an expert in clinical chemistry, computer programming, systems design for laboratory operations, and automation of analytical instruments. He designed and closely supervised fabrication of an automated enzyme analyzer with temperature control to 0.02°C. His informed consultations were much sought by research scientists and clinicians alike. He wrote lucidly, and unselfishly shared his new knowledge and research findings with all. Ernie was a dedicated pioneer; he never complained or hesitated to respond, even in the middle of the night, when called out because the computer broke down, or when called to interpret an emergency test result, or when rain flooded the computer room, and while covering the machines with tarps, he would joke with his night staff that they had the only computer in the world that could run underwater.

Dr. Cotlove was a founding member of ACLPS. Following his untimely death in 1970, ACLPS established a Cotlove Lectureship. This award is presented to a scientist (member or non-member of the academy) for outstanding contributions to the science of laboratory medicine.

2023 Ernest Cotlove Lecture & Award

Amy Mathers, MD (UVA) — see p. 12

Ellis Benson Lectureship

Ellis Starbranch Benson was born October 28, 1919, in Xuchanq, Henan, China, where his parents were American missionaries. Xuchenq is a provincial market city on the north China plain, south of Beijing. He spent most of his boyhood in China attending a boarding school for missionary children, a very pleasant school on a mountain. Those years strongly influenced his view of the world. After graduating from high school, he sailed to America.

In the U.S., Ellis enrolled in a small junior college in Wahoo, Nebraska, intending to become a chemical engineer. He soon realized that engineering was not for him and switched to a pre-med program. However, chemistry became a lifelong interest. He completed college at Augustana in Rock Island, Illinois, and then entered medical school at the University of Minnesota in the fall of 1941. Medical school was an eye opener. He was overwhelmed by the size of the University and the sophistication of his classmates, most of whom had taken their pre-med at the University of Minnesota. Ellis studied much harder than ever before and to his surprise at the end of the year he was ranked third in his class. (Medical students were ranked in those halcyon days).

Ellis graduated from medical school in September of 1944 because of an accelerated war time program. He left for his internship at Cincinnati General Hospital. After an internship, he entered the Army as a medical officer in July of 1945. The war ended in August and his orders to go to the Far East were cancelled. Instead, he was sent to Germany, where he met his wife, Ann, the daughter of an American War Department civilian working with the U.S. Army Engineers. They were married in Hanau, Germany, in April of 1947.

Ellis and his wife returned to the U.S. in May, and Ellis entered residency under Professor E.T. Bell in the University of Minnesota's Department of Pathology. There were two new residents in pathology that year, Don Gleason and Ellis Benson. Dr. Bell decreed that after one year in anatomic pathology, one of them would go to laboratory medicine for a year. Accordingly, a coin was tossed by the chief resident and, consequently, Ellis went to laboratory medicine and Don moved to anatomic pathology. Don went on to distinguish himself as the author of the Gleason system of staging prostate cancer, which is now used worldwide. Ellis spent a delightful year in laboratory medicine, mostly in chemistry with G.T. Evans. After laboratory medicine, he began a residency in medicine.

In 1949, Ellis received a call from Dr. Evans offering him an instructorship in the laboratory medicine section of the Department of Medicine at the University. He accepted quickly and started in October of 1949. In 1959 laboratory medicine became a separate department with Dr. Evans as chairman. Ellis Benson's research interests were in heart muscle proteins, notably actin and myosin. He soon realized that he would need more training in protein chemistry, so in 1957, he went to Denmark with his family for a year at the Karlsberg Laboratory in Copenhagen, where he worked with Kai Linderstrom-Lang. It was a decisive year for Ellis. Lindstron-Lang was a world renowned protein chemist who helped him to embark on a new research program that used hydrogen exchange to help understand the basic structure and motility of certain proteins. Back at Minnesota, Ellis became a professor in 1962 and then department head in 1966 when Dr. Evans retired. In 1965 a small group got together and planned a new society in academic laboratory medicine. The group was made up of George Williams, Ernest Cotlove, David Seligson, Jon Straumpfjord, and Ellis Benson. The society

Continued, next page

Ellis Benson Lectureship | continued

that became ACLPS came into being in 1966 at a meeting of a larger group in Bethesda, where Ellis was chosen to be its first president. In 1970, Ellis spent a sabbatical year at the University of Rome in the Laboratory of Eraldo Antonini. As a result, he embarked on a research program on hemoglobin structure and red cell biology. In 1973, Ellis was asked to become chair of a newly merged Department of Laboratory Medicine and Pathology. The merger succeeded with great help from the faculty of both former departments. Ellis became a trustee of the American Board of Pathology in 1970 and its president in 1982. His area of major responsibility was chemical pathology. He retired as department head in 1989 and as professor in 1990.

2023 Ellis Benson Lecture & Award

Sarah Wheeler, PhD — See p. 13

Paul E. Strandjord Young Investigator Grant

Paul E. Strandjord, MD (1931-2001) was the founding Chair of the Department of Laboratory Medicine at the University of Washington School of Medicine. The grant program named in his honor is designed to encourage young investigators to consider a career in academic laboratory medicine. Residents, fellows, and students in a doctoral program in health sciences, participating in research with a member of ACLPS or sponsored by an ACLPS member, are eligible. Students in programs leading to non-doctoral degrees conducting research with an ACLPS member may be considered upon written request from the ACLPS sponsor to the director of the Young Investigator Awards Program. Proposed research may be clinical, translational, basic science, quality improvement, and/or regulatory.

2022 Grant Recipient Presentations

Edward Lee, MD, PhD; Jun Liu, MD, PhD; Rebecca Treger, MD, PhD — See p. 12

2023 Grant Recipients

Cheryl Maier, MD, PhD; Kayode Balogun, PhD; Kai Rogers, MD, PhD; Nicholas Spies, MD

Abstracts

Young Investigator Abstracts – A Sessions

Young Investigator Abstracts – B Sessions

Poster Abstracts

Abstract Speaker Disclosure

Thomas Durant (B12): Consultant (Abbott, Roche)

No other conflicts were reported by abstract speakers.

Abstracts | Young Investigator A Sessions

Session A1: Coagulation
A01

Performance of a Direct Oral Anticoagulant Removal Reagent, DOAC-Stop™, for Lupus Anticoagulant Testing

Mark Girton[1], Mary Acker[2], Lindsay Bazydlo[1]

[1]*Department of Pathology, University of Virginia, Charlottesville, Virginia,* [2]*Core Laboratories, University of Virginia, Charlottesville, Virginia*

Objective: Routine use of direct factor Xa inhibitor (direct oral anticoagulant; DOAC) therapy necessitates a modified lupus anticoagulant (LAC) testing method for this population. To remove interfering DOACs in specimens, DOAC-Stop™ treatment was used on LAC specimens to assess for antiphospholipid syndrome (APS) without altering patient's anticoagulation treatment. **Methods:** DOAC-Stop™ was evaluated with our LAC testing panel with dilute Russell viper venom time (dRVVT), and Silica Clotting Time (SCT) assays, both of which activate coagulation. DOAC-Stop™ beads were used for pretreatment by addition and rocking for 5 minutes, followed by 5000 rpm centrifugation for 5-minutes. Treated plasma supernatant was used for a screen, confirm (addition of phospholipid), 50:50 mix (addition of reagent plasma with coagulation factors), and confirm 50:50 mix phases of testing. The Total Ratio (TR; ratio between screen and confirm ratios relative to mean of normal ranges) was calculated and used per the package insert for interpretation. Implementation data was assessed for interpretation differences between groups with and without DOAC-Stop™ treatment. **Results:** Patients being tested for APS by LAC assay with and without DOAC therapy were included. DOACs included apixaban or rivaroxaban. Primary interpretations included no evidence of a LAC (NELAC), evidence of LAC, and results more consistent with coagulation factor deficiency. The effectiveness of DOAC removal was established by spiking NELAC samples with apixaban and treating with DOAC-Stop™, resulting in removal of anti-factor Xa activity. An apixaban spiking study with NELAC and LAC patient specimens with LAC testing before and after DOAC-Stop™ treatment demonstrated unchanged interpretations. In a test modification study, Rivaroxaban resulted in positive dRVVT interpretations in nine of ten patients. All but one became negative after DOAC-Stop™ treatment. Two SCT interpretations became positive after treatment. Apixaban resulted in two positive dRVVT interpretation in nine patients, one of which became negative after DOAC-Stop™ treatment. SCT interpretations remained unchanged. Review of implementation data (n=78) with nine patients on DOACs having DOAC-Stop™ treatment demonstrated similar patterns of test interpretation. Interpretations included: "no evidence of a LAC" in 53% (n=41) without and 55% (n=5) with DOAC-Stop™, "Does not meet criteria" in 17% (n=13) without and 11% (n=1) with DOAC-Stop™, "Evidence of a LAC" in 21% (n=16) without and 33% (n=3) with DOAC-Stop™. The remaining eight patients without DOAC-Stop™ treatment had interpretations including factor deficiency, warfarin effect, equivocal, or concerning for interference. **Conclusion:** Patients on DOACs benefit from DOAC-Stop™ –enable LAC testing for APS assessment. Data analysis demonstrates that DOAC-Stop™ effectively removes DOAC interference in the majority of tests with similar rates of major interpretation categories. LAC testing and interpretation for patients on DOAC therapy shows promise with novel approaches and reagents such as DOAC-Stop™, though interpretative challenges with false-positives and false-negatives continue.

Session A1: Coagulation
A02

Quality Analysis of Lupus Anticoagulant Testing: Indeterminate and Interference

Timothy Bell, Morayma Reyes Gil, Lauren (Ashley) Duckworth, Peter Mannion, Sarah Alnaqshabandi, Narendra Bhattarai

Cleveland Clinic, Cleveland, Ohio

Lupus anticoagulant (LA) testing is a commonly performed test within hemostasis laboratories. Criteria for diagnosing a LA based on the International Society on Thrombosis and Hemostasis are: prolonged phospholipid-dependent (PD) clotting test, evidence of an inhibitor, evidence the inhibitor is PD, and exclusion of specific inhibitors. At our academic institution, we analyzed Lupus anticoagulant results to establish common sources of drug interference (DI), identify causes of indeterminate results, and evaluate if repeat testing was performed on patients with an initial indeterminate test. At this institution, Lupus anticoagulant evaluation includes activated partial thromboplastin time (aPTT), Anti-Xa activity, Thrombin Time (TT), diluted Russell Viper Venom Time, hexagonal phase phospholipid assay, and Platelet Neutralization Procedure. Samples with Anti-Xa activity >0.1 IU/mL and/or elevated TT are treated with hepzyme; if the Anti-Xa activity or TT does not correct, testing is not completed. Samples with elevated aPTT undergo an immediate and incubated mixing study (MS). Samples are considered positive (POS) for LA if there is a positive screening test (+ST), +MS, and evidence of PD in at least one assay. Tests are resulted as indeterminate (IND) with a +ST and either +MS or +PD. LA results are reported as unlikely (UNL) if only a single phospholipid panel is positive without +ST or +MS, and negative (NEG) if the ST, MS, and PD assays are all negative. Patients with indeterminate LA testing are recommended to have repeat LA testing after 12 weeks. A total of 3025 cases were identified over the 18-month period (July 2020 – December 2021). The majority of cases were interpreted as NEG (2310; 76%) followed by 8% POS (229), 6% IND (174), and 1% UNL (34). While the majority of IND met the ST (99%) and PD (71%) criteria, only 32% were +MS, indicating failure of an inhibitor detection in the mixing study is the major factor preventing an IND from becoming positive. Within the IND group, only 25% (43) underwent the recommended repeat LA testing. The results of repeated 43 IND tests are as follows: 16 NEG, 4 POS, 19 IND, 3UNL, 1 DI. While a significant proportion of IND repeated testing became negative, a majority remained IND, arguing for more comprehensive LA testing. This quality study demonstrates the majority of patients at this institution who receive an interpretation of IND LA do not undergo the recommended repeat testing, underscoring the importance of follow-up and education to standardize care. Prospective studies maybe needed to elucidate the clinical significance of IND LAs. Additionally, 278 (9%) cases were canceled due to drug interference, the majority (192; 69%) due to direct oral anticoagulants (DOAC). Testing for LA in patients actively receiving DOACs should be discouraged. Alternatively, methods to remove DOAC interference should be standardized.

Session A1: Coagulation
A03

Using an Agonist Panel and Aggregation to Assess Antiplatelet Therapy in Mice

Dominique Gordy, Richard Francis, Elizabeth Stone

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Platelets play a crucial role in hemostasis. For cardiovascular and stroke prophylaxis, patients are commonly placed on either single or dual antiplatelet drugs, such as aspirin and/or clopidogrel. Here we outline a mouse model examining antiplatelet therapy and the resulting changes in platelet activation and aggregation. Using commercially available transgenic mice with platelets expressing green fluorescent protein (GFP) or red fluorescent protein (RFP), endogenous platelets were inhibited with a single, dual, or control antiplatelet treatment. We used 100µg aspirin/g mouse or 50µg clopidogrel/g mouse for a single dose; dual antiplatelet therapy was a combined dose of 100µg aspirin/g mouse and 50µg clopidogrel/g; control treatment was DMSO alone. One hour after treatment, whole blood (WB) was collected by aseptic cardiac puncture and mixed in the following groups: aspirin treated RFP and GFP WB, clopidogrel treated RFP and GFP WB, aspirin and clopidogrel treated RFP and GFP WB, control treated RFP and GFP WB. Each combined sample was then treated with a panel of agonists: no agonist, 0.5U/mL thrombin, 20µM ADP, and 500µg/mL arachidonic acid. Thrombin samples were activated for 2 minutes at room temperature while ADP and arachidonic acid samples were activated for 10 minutes at 37°C. Platelets were labeled with anti-CD41a to label all platelets and anti-CD62P to label activated platelets. Aggregation is measured as double-colored GFP and RFP platelet events. Compared to control mice, mice treated with antiplatelet agents demonstrated statistically significant decreases in activation following thrombin administration (ranging from 90% to 83% activated); there was no significant difference in platelet aggregation following thrombin among the samples from different antiplatelet therapies. Following ADP activation, clopidogrel treatment decreased platelet activation (1% activation) compared to control (3% activation) and aspirin-treated (5% activation) mice with no additional decrease in dual treatment (1% activation); unexpectedly, aspirin treatment alone or dual therapy decreased platelet aggregation with ADP (15% and 17% aggregated, respectively) compared to control and clopidogrel (23% and 27% aggregated, respectively). Finally, after arachidonic acid activation, aspirin treatment significantly decreased activation (7% activated) compared to control (20% activated), while clopidogrel decreased activation more than that of aspirin (3% activated), with no additional decrease from dual therapy (3% activated). Though not significant, aspirin treatment (1.4% aggregation) and dual therapy (1.2%) demonstrated a trend with decreased platelet aggregation following arachidonic acid activation compared to control (1.8% aggregation) and clopidogrel-treated platelets (3.2%). These data presented here show a novel application of platelet activation and aggregation of GFP and RFP platelet populations in a mouse model following aspirin and/or clopidogrel treatment. This model can be applied generally to other drugs and disease models for platelet dysfunction using additional markers for platelet activation. Additionally, these experiments can be used to further investigate the function of transfused murine platelets.

Session A1: Coagulation
A04

Use of Plasmapheresis in Heparin Induced Thrombocytopenia in Patients Undergoing Urgent Cardiac Surgery

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Heparin Induced Thrombocytopenia (HIT) is a potentially life-threatening but uncommon disease process characterized by IgG antibodies that recognize platelet factor 4/heparin immune complexes causing thrombocytopenia and thrombosis. Although therapeutic plasmapheresis (PLEX) appears to be effective, protocols regarding how and when to institute PLEX remain elusive. At our institution, we put together a standardized approach to assess the interventional success across patients that included 1 plasmapheresis procedure per day over 4 days, processing one plasma volume and using thawed plasma as the replacement fluid. Treatment effectiveness was evaluated by pre- and post-interventional HIPA OD levels and platelet count. Treatment aim was to decrease the HIPA OD to less than 0.6 and obtain a normal platelet count.
The aim of this study was to design a protocol for PLEX to address urgent need for patients with HIT for which heparin is planned for intraoperative cardiac surgery requiring cardiopulmonary bypass (CPB) anticoagulation. We retrospectively examined the medical records of 2 HIT-positive patients who underwent PLEX prior to cardiac surgery at our large quaternary care hospital. Both patients had a 4Ts score of 5, with a medium probability of disease. One patient's HIT was confirmed by a positive serotonin release assay (SRA). The second patient had persistently negative confirmatory test but was deemed clinical HIT.
The first patient is a 53-year-old female, who was admitted for mitral valve replacement, aortic valve replacement, and tricuspid valve repair. She was confirmed HIT by positive SRA. Three sessions of PLEX were performed on consecutive days. Her HIPA (heparin induced platelet antibody) O.D. value decreased from 1.925 to 0.534 and platelet counts normalized. The second patient is a 73-year-old male, who was admitted for LVAD implantation and LV thrombus resection. Two sessions of PLEX were performed on consecutive days. His HIPA O.D. value deceased from 1.261 to < 0.4 (negative) and platelet counts normalized. For both patients, the last PLEX procedure was performed the day of surgery, and the cardiac surgical procedure was completed successfully.
Based on these 2 patients, we have proposed a protocol for PLEX in HIT patients as follows: daily plasmapheresis x 4 days will be performed until the OD has decreased to less than 0.6 and platelet count has normalized. Each plasmapheresis will consist of the processing of one plasma volume, using thawed plasma as the replacement fluid. The last plasmapheresis will occur on the day of surgery prior to surgery. Further assessment will be performed if the targeted parameters have not been met by the 4th plasmapheresis procedure.

In conclusion, we present 2 patients with HIT who benefitted from PLEX prior to cardiac surgery under CPB. We will adopt the protocol used for these 2 patients as our standard of practice moving forward.

Session A1: Coagulation
A05

Anticoagulation Management in Patients Tested for Heparin-induced Thrombocytopenia in the Cardiothoracic Intensive Care Unit Diverges from Expert Guidelines

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Heparin-induced thrombocytopenia (HIT) is a rare, life-threatening complication in patients receiving heparin products. Clinical scoring tools, such as the '4T' score, aim to help identify patients at risk for HIT and are recommended by expert guidelines. For example, the American Society of Hematology (ASH) recommends that patients with an intermediate or high-risk 4T score are presumptively treated for HIT by withdrawing heparin and starting an alternative anticoagulant. At our institution, laboratory HIT testing involves an in-house latex immunoassay (LIA) that, if positive, reflexes to a send-out serotonin release assay (SRA) at the Blood Center of Wisconsin. This confirmation may take several days to result, underscoring the importance of presumptive treatment. Anecdotally, we have observed that clinicians have expressed reservations about the use of the 4T score in the cardiothoracic intensive care unit (CTICU). These reservations may lead to increased HIT testing in patients with low 4T scores and delays in the initiation of alternative anticoagulants. We set out to objectively determine if clinical practice in the CTICU is aligned with ASH guidelines. To do so, we used anticoagulant usage as a proxy for medical decisions made at the time of order for HIT laboratory testing. Data was extracted from the electronic medical records of all patients who were admitted to the CTICU between 5/2018 and 7/2022 and administered a heparin product (n = 1,602). Patients that were not tested for HIT (n = 1,449) were excluded. The remaining patients' (n = 153) medication record timings were normalized such that the time of their first LIA was set to zero to allow for relative comparisons. 25 (16%) of the LIAs were positive, of which 5 (20%) were confirmed by SRA. Of the 153 patients, 136 (89%) received heparin within 24 hours prior to LIA order, while 6 (4%) were already on alternative anticoagulation (bivalirudin). Of the patients on heparin prior to LIA, 18 (13%) were switched to bivalirudin upon LIA order, 66 (49%) had heparin discontinued without an alternative, and 52 (39%) were continued on heparin. Our results suggest that the prevalence of HIT in this cohort is 3.3% by SRA, much lower than the expected pretest probability estimated for intermediate- and high-risk 4T scores in published meta-analyses. In addition, the observed anticoagulation practices varied widely and diverged from ASH guidelines, where only 17% of patients were on alternative anticoagulation when the testing was ordered. Future work will investigate these patterns across LIA positivity and 4T scores while attempting to address the clinical outcomes of these treatment decisions.

Session A2: Toxicology
A06

Phosphatidylethanol as a Biomarker to Assess Alcohol Exposure in Women of Reproductive Age Using Retrospective Data from a Reference Laboratory

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Alcohol consumption during pregnancy may cause fetal alcohol spectrum disorder (FASD), which is a preventable disorder. Prenatal alcohol exposure during the first trimester of pregnancy is deemed most disruptive to the developing fetus. Pregnant women may be screened for alcohol use through self-reported measures. These subjective methods are known to underreport drug use. Therefore, a reliable method to detect and monitor alcohol use during pregnancy is needed. Phosphatidylethanol (PEth) is a specific biomarker associated with alcohol consumption that can be used to differentiate social drinking from heavy alcohol use. The predominant PEth homologues are PEth 16:0/18:1 (POPEth) and PEth 16:0/18:2 (PLPEth), which account for 37-46% and 26-28% of the total PEth homologues, respectively. PEth can reflect alcohol intake up to several days to weeks after consumption. The aim of this study is to investigate the prevalence of positive PEth samples in women of reproductive age to determine whether testing for PEth should be assessed in a three-month checkup in pregnant women. The first objective is to perform a retrospective study on the direct alcohol biomarker, PEth, to evaluate the true positivity rates of alcohol use in females and in women of reproductive age (14 - 44 years old) using retrospective data analysis from a reference laboratory. The initial data analysis demonstrated the positivity rate of PEth in females (N = 66,306) to be 32% for POPEth and 28% for PLPEth. Further retrospective data analysis of PEth in women of reproductive age (N = 19,366) was performed and the positivity rate of PEth in this population was quite similar between the ages of 27 to 40 years old, at around 35%. The data shows that the positivity rate of PEth in women of reproductive age (~35%) is slightly above the positivity rate for all females (~30%). These percentages are significantly higher than what is reported in the 2020 National Survey on Drug Use and Health (NSDUH). The NSDUH reported that 10.6% of pregnant women used alcohol in the past month. The second objective is to conduct a laboratory study where we will measure PEth concentrations by mass spectrometry using residual whole blood specimens from females in an OB/GYN clinic and compare the positivity rates to those determined by the retrospective analysis. This study will provide the opportunity to educate women of reproductive age on drinking during pregnancy and the long-term effects of alcohol use.

Abstracts | Young Investigator A Sessions

Session A2: Toxicology
A07

Lorazepam Detection with Urine Benzodiazepines Screening Tests: Not all Tests are Created Equal

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Lorazepam belongs to the benzodiazepines family of drugs and is one of the commonly used anti-anxiety medications in the US. In clinical practice, immunoassay screening tests are used to monitor compliance, detect abuse and in cases of drug overdose. Many clinicians rely on benzodiazepine immunoassay screening tests to detect lorazepam due to the test availability on automated clinical analyzers, short turnaround time and cost efficiency. However, compromised test sensitivity often leads to erroneous results. In this study, we used mass spectrometry to establish the lorazepam cross-reactivity threshold in two commonly used benzodiazepine screening tests: the Abbott ARCHITECT cSystem 16000 and NexScreen Drug Screen Cup. **Methods:** Mass spectrometry testing was performed at a major reference laboratory. Lorazepam-positive patient urine at concentrations of 320 ng/mL and 4,895 ng/mL were tested concurrently by two immunoassay methods. The Abbott ARCHITECT is a semi-quantitative assay with a positivity cut-off of 200 ng/mL. According to the manufacturer's instructions for use (IFUs), the cross-reactivity threshold of the test is equivalent to a lorazepam concentration of 650 ng/mL. The NexScreen Drug Screen Cup is a lateral flow immunoassay used as a point-of-care (POC) test. The positivity cut-off of this test is 300 ng/mL; per IFUs, the cross-reactivity threshold of this test to lorazepam is 3,900 ng/mL, and 5,000 ng/mL for lorazepam-glucuronide, a drug metabolite. To determine the test sensitivity of the NexScreen test, patient specimen (4,895 ng/mL) was diluted at 1:5, 1:10, 1:20, 1:50, and 1:100, targeting the lorazepam concentrations of 979, 490, 245, 98 and 49 ng/mL respectively. To determine the sensitivity of the immunoassays to the parent molecule vs the metabolite, pre-screened negative urine was spiked with lorazepam or lorazepam-glucuronide at a concentration of 650 ng/mL, 5000 ng/mL, and 10000 ng/mL. **Results:** Abbott ARCHITECT failed to detect lorazepam in both patients, while the NexScreen resulted in positive benzodiazepine screen results for both patient specimens. All lorazepam-spiked specimens tested positive on both methods. However, all lorazepam glucuronide-spiked specimens tested negative on Abbott ARCHITECT and positive on NexScreen cup. The highest dilution detected by NexScreen was 1: 20, equivalent to approximately 245 ng/mL of lorazepam. **Conclusion:** Our findings suggest that the ARCHITECT benzodiazepine assay should not be used to screen patients on lorazepam, given its inability to detect the major metabolite, lorazepam glucuronide. Whenever available, a mass spectrometry method is always preferred. The results of our study demonstrated that in a specific patient population, where the likelihood of positive lorazepam test is high, the NexScreen cup is a viable, cost-effective alternative due to its excellent sensitivity.

Session A2: Toxicology
A08

Evaluation of Siltuximab and Tocilizumab Analytical Interference on Interleukin 6 Measurements

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Background: Interleukin 6 (IL-6) plays important roles in both innate and adaptive immunity, while dysregulated persistent production of IL-6 is involved in pathological development of various diseases associated with inflammation. Targeting the IL-6 pathway has led to many innovative treatment approaches. Siltuximab and Tocilizumab are monoclonal antibodies targeting IL-6 and IL-6 receptors respectively and have been FDA-approved for treatment of Castleman disease (Siltuximab), a rare lymphoproliferative disorder characterized by hyperproduction of IL-6 with an unknown prevalence, autoimmune diseases such as rheumatoid arthritis (Tocilizumab), and both shown potential as treatment for cytokine release syndrome in hospitalized COVID-19 patients. However, the presence of siltuximab can interfere with IL-6 assays, leading to the use of C-reactive protein (CRP) as a surrogate marker to monitor its efficacy. **Aim:** To evaluate potential Siltuximab and Tocilizumab antibody interference on IL-6 measurements in three different IL-6 protein immunoassays. **Method:** Serum or EDTA plasma sample pools with different IL-6 concentrations ranging from low (2.3 – 11.1 pg/mL, around the reference interval cut-off for each assay) to high (18.5 – 1142 pg/mL), above reference interval cut-off for each assay) were utilized. Various concentrations of Siltuximab or Tocilizumab were spiked into the sample pools (at 10% of total volume) to achieve final concentrations up to 600 µg/mL and up to 300 µg/mL, respectively. Sample spiked with 10% saline were used as no-drug control. Three assays were used to measure IL-6 concentration: Beckman Access IL-6 assay on UniCel DxI 800 (Beckman Coulter), V-PLEX Plus human IL-6 assay on QuickPlex SQ120 (Meso Scale Diagnostics), and a Luminex cytokine panel assay developed in house (R&D systems) with upper reference interval limits of 6.4,1.8 and 5 pg/mL respectively. **Results:** Siltuximab interfered with the measurement of IL-6 for all three assays. A significant interference (> 20% reduction) was observed at even a very low siltuximab concentrations in all three assays (0.05 µg/mL). In the presence of 5 µg/mL or greater Siltuximab, a maximum reduction of 93%, 83%, and 40% was observed for Beckman Access, R&D Luminex assay, and V-PLEX Plus Mesoscale assay, respectively. Tocilizumab did not interfere with the measurement of IL-6 in the three assays when serum was spiked with up to 300 µg/mL of the drug. **Conclusion:** Siltuximab falsely reduce the measured IL-6 concentration on all three immunoassays tested in this study to differing degrees, whereas Tocilizumab does not. Consider the therapeutic range of Siltuximab (84 to 332 µg/mL) for treatment of Castleman disease, and a half-life of 20.6 days, measurement of IL-6 may not be useful in Siltuximab treated patients for an extended time-period.

Session A2: Toxicology
A09

Take Precaution with Choice of Pastry: Poppy Seed-containing Products Cause Significantly Positive Results in Urine Drug Tests

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Background: Chronic pain management programs utilize urine drug testing to ensure patient compliance. Because treatment can be discontinued if diversion or misuse occurs, it is imperative to carefully interpret each urine drug screen, particularly with respect to potential interferences and exposure to opioid-containing foods. Poppy seeds, derived from the opium-producing poppy *Papaver cominferum L.*, are used widely in food products. While the seeds themselves do not contain opiates, during the harvesting process, the seeds can be contaminated with poppy latex, which does contain numerous alkaloids, including morphine and codeine. Published guidelines suggest urinary codeine concentrations exceeding 300 ng/mL, together with a morphine-to-codeine ratio <2, were most consistent with codeine use, effectively ruling out poppy seed ingestion.
Methods: To assess the validity of these guidelines, we performed an internal quality improvement project, which consisted of 15 participants split into three groups. Each group consumed one of three different poppy seed-containing food products (i.e., poppy seed muffin, poppy seed bagel, or poppy seed roll). Participants collected urine samples midstream at baseline and at 3, 6, and 24 hr after ingestion. Opiates in urine were qualitatively detected via immunoassay (Beckman Coulter AU 680) and quantified by liquid chromatography-tandem mass spectrometry.
Results: For the group of participants that ingested a poppy seed roll, which contains a thick paste made from poppy seeds, all urine specimens at all time points had positive opiate immunoassay results, while the group of participants that ingested a poppy seed muffin had positive immunoassay results only at the 3- and 6-hr time-points. In contrast, all but one participant for all time points after consumption of a poppy seed bagel had negative immunoassay results. Codeine and metabolites were observed in all three groups; however, codeine concentrations were significantly higher after ingestion of a muffin or a roll, notably resulting in levels well above 1,000 ng/mL and 10,000 ng/mL of codeine and codeine-6-glucuronide, respectively. Codeine:morphine ratios ranged from 100 to 250:1 in poppy seed muffin and roll groups at 3- and 6-hour time points. There was significant variability in urine opiate concentrations among all participants in each group at each time-point.
Conclusions: Although urine opiate concentrations vary due to the metabolism of the individual as well as the origin, processing, and preparation of the poppy seed product, it is clear that previously established guidelines for interpreting urine codeine concentrations may no longer be appropriate to rule out poppy seed ingestion. When evaluating urine drug test results for chronic pain management, providers should interpret results with caution and ultimately recommend that patients generally avoid poppy seed products to prevent the risk of care mismanagement.

Session A3: Microbiology
A10

Enteric Pathogens within the Men Who Have Sex with Men Population, Associated Risk Factors, and Provider Vigilance: Analyzing Three Years of Biofire® Data with Retrospective Chart Review

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Men who have sex with men (MSM) can be at a higher risk for enteric pathogens due to sexual transmission, which has been known since the 1970s but has garnered greater attention in recent years due to the global spread of multi-drug resistant enteric organisms. This has given impetus for identifying specific risk factors and for providers to be vigilant of those at highest risk so they can appropriately treat and educate patients. The purpose of this study was to within the MSM population, further characterize the risk of enteric pathogens, assess specific risk factors associated with enteric pathogen acquisition, and evaluate provider vigilance of the increased risk. Over approximately a thirty-four month period at a major tertiary metropolitan medical system, this study retrospectively looked at 436 BioFire® FilmArray® Gastrointestinal Panel results in 361 patients documented as MSM. A concurrent chart review was performed, which included specific sexual behaviors and if providers charted a sexual history in the visit associated with the BioFire® order. Overall BioFire® positivity rate in this MSM population was 62% compared to a general population positivity rate of 33.5% found in a prior study at the same institution. Enteropathogenic *Escherichia coli*, *Shigella*/enteroinvasive *E. coli*, enteroaggregative *E. coli*, norovirus, *Giardia,* and *Campylobacter* were the most commonly identified pathogens. There was no significant difference in the positivity rate between individuals with HIV compared to those without HIV, although those with HIV were more likely to be positive for *Shigella* and those without HIV were more likely to be positive for *Giardia*. Compared to those who were not, patients charted as sexually active had a significantly increased odds ratio of a positive result, and anilingus was the sexual behavior with the highest odds ratio. Housing status was not a statistically significant risk factor for a positive result. Providers overall charted any type of sexual history in 40.6% of cases with HIV/infectious disease providers significantly more likely to do this compared to other specialties. This study demonstrated that sexual transmission of enteric pathogens within MSM is ongoing and patients can be at risk regardless of HIV status. Certain sexual behaviors like anilingus confer higher risk. This study also suggests that many providers may not be aware of the risk for enteric sexual transmission within MSM as less than half of them charted a sexual history when ordering a BioFire® panel.

Session A3: Microbiology
A11

Multilocus Sequence Typing of Emerging Azole-Resistant Candida auris Isolates from Critically Ill Patients in a New York City Medical Center

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Candida auris has developed into a slow-moving global pandemic since its emergence in 2009, particularly as a source of nosocomial infection amongst immunocompromised and critically-ill patients. According to CDC data, *C. auris* emergence has accelerated in the US during the COVID-19 pandemic and has garnered particular attention for its high level of resistance to multiple classes of antifungals. *C. auris* has been categorized into five genetically diverse clades, each with unique antifungal drug resistance patterns. We have observed a sharp increase in cases identified at our tertiary medical center in New York City over the past three years. In this study, we designed a set of *C. auris*-specific oligonucleotides to determine the clonality of isolates through Multilocus Sequence Typing (MLST) of four genetic loci known to have a high level of divergence amongst Candida species. From 2020 through 2022 we identified 22 patients with *C. auris* bloodstream infection at our institution by Matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) and performed MLST on isolates that were available from 19 patients. We assessed four genetic loci: *ITS1/ITS2*, *D1/D2, RPB1* and *RPB2; ERG11* was included to assess for mutations associated with fluconazole resistance. We found that the number of blood stream infections increased from 2 cases in 2020 to 12 in 2022. Our MLST results showed that all *C. auris* isolates from blood and body fluids belong to CDC-defined Clade 1c, which carries the ERG11 gene mutation resulting the amino acid substitution K143R in 14-α-Demethylase associated with fluconazole resistance. These isolates also demonstrated fluconazole resistance by *in vitro* testing (19/19), amphotericin resistance was present in 44% of isolates with available data (7/16), and all isolates were susceptible to micafungin (19/19). Of 19 patients with blood cultures positive for *C. auris*, 13 (68%) were in a critical care setting at time of collection, 17 (89%) had been in an ICU during the same admission, and 8 (42%) expired within 3 months of *C. auris* positivity. MLST is considered a relatively fast and inexpensive method of sequence-based strain typing and has recently been applied to assessing the clonality of *C. auris* isolates. We show that the use of *C. auris*-specific oligonucleotides for sequencing, rather than those derived from other Candida species, produces high quality data for MLST, as well as the detection of specific mutations involved in antifungal resistance, such as ERG11. Further assessment is needed by the gold standard in sequence typing, Whole Genome Sequencing (WGS), to confirm our analysis of clonality here. MLST may therefore represent a useful tool in understanding the interrelatedness of invasive *C. auris* infections in hospitalized patients as well as inform clinical decision-making around infection control and empiric antifungal therapy.

Session A3: Microbiology
A12

Evaluation of Clinically Tractable Methods for Treponema pallidum DNA Extraction from Whole Blood

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Background: The steady growth in syphilis cases in the US, including congenital disease, prompted us to develop and validate a nucleic acid amplification test (NAAT) for its causative agent, *Treponema pallidum* (*T. pallidum*), with an analytical sensitivity of 7-10 genomes per reaction. To expand the clinical utility of the assay, we sought to validate a method for extraction of *T. pallidum* nucleic acids from EDTA-anticoagulated whole blood with a limit of detection (LOD) between 100-300 organisms/mL. **Methods**: *T. pallidum* Nichols, SS14, and Chicago strains were cultured *in vitro,* and titers estimated by darkfield microscopy. Cells were used fresh or after freezing in 10% DMSO and spiked into residual EDTA-anticoagulated whole blood at concentrations ranging from 250 to 10,000 organisms/mL. We evaluated the following lysis methods: incubation in manufacturer-provided NUCLISENS lysis buffer (Biomerieux), a clinically validated method for both instruments; treatment with buffer ATL (Qiagen); a -80C freeze-thaw cycle; bead-beating; recombinant lysozyme; and combinations of freeze-thaw, bead-beating, and lysozyme. Nucleic acid extractions were performed on the EZ2 (Qiagen) and easyMAG (Biomérieux) instruments using manufacturer-provided kits. Total nucleic acid extraction was performed following clinically validated protocols: incubation in NUCLISENS lysis buffer followed by NUCLISENS (easyMAG) or the Virus Mini Kit 2.0 (EZ2) using recommended or 2X specimen volumes. Genomic DNA was extracted with the gDNA blood kit. Additionally, we evaluated concentration by centrifugation and a validated RBC lysis protocol for use with buffer ATL and the Virus Mini Kit 2.0. Eluates were interrogated with the established clinical assay and scored as positive or negative. **Results**: Lysis of manufacturer-recommended whole blood volumes in NUCLISENS lysis tubes resulted in detection rates of 100% at 1000 organism/mL (~1.5 – 3 organisms/reaction), 72% at 500 organisms /mL, and 56% at 250 organisms/mL. Doubling the sample volume in NUCLISENS lysis tubes resulted in no detectable analyte. Lysis with buffer ATL resulted in >95% detection at 1000 organisms/mL. Genomic DNA extraction failed to detect analyte at 10,000 organisms/mL unless pre-treated with mechanical or enzymatic lysis: 30-60min at -80C, 30sec bead-beating, or 20U/mcL of recombinant lysozyme were required for successful detection. Lower concentrations of lysozyme had 50% detection rates. Concentration by centrifugation and RBC lysis was successful but did not show a difference in Ct values relative to centrifuged samples without RBC lysis (27.3-31.2 vs 27.3 – 33.6). Inhibition was not observed. **Conclusions**: Molecular detection of *T. pallidum* DNA from blood is possible but insensitive for clinical application, similar to prior reports. Extraction of *T. pallidum* nucleic acids requires a lysis step compatible with bacteria. Multiple simple methods are compatible with the clinical NAAT. Future work will evaluate pre-analytical concentration of bacteria prior to lysis and extraction.

Session A3: Microbiology
A13

Antimicrobial Susceptibility Patterns among a Large, Nationwide Cohort of Chryseobacterium Species Clinical Isolates

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Background: *Chryseobacterium* species are ubiquitous in nature that can be found in soil, water, sinks, and medical devices. They have been implicated in various infections including ventilator-associated pneumonia, catheter-related bloodstream infections (CRBSI), skin and soft tissue infections, and meningitis. *C. indologenes* has been shown to possess an extended-spectrum beta-lactamase (ESBL) and metallo-β-lactamase (MBL) that render it resistant to most antibiotics. Antimicrobial susceptibility testing (AST) data are required to help clinicians choose effective empiric antibiotics and to investigate potential resistance mechanisms. **Methods:** *Chryseobacterium* spp. identification was determined prior to submission by client laboratories or performed in our laboratory by MALDI-TOF (Bruker Biotyper) or 16S rRNA gene sequencing. AST was performed on *Chryseobacterium* species isolates received from across the United States between April 2004 and December 2018. AST was performed using custom-made broth microdilution panels, and minimal inhibitory concentrations (MICs) were interpreted using CLSI M100 MIC breakpoints for non-*Enterobacterales* organisms. Isolates from a range of clinical specimens including blood, respiratory, wound, tissue, bone, and body fluids were included. Quality control was performed using *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853. Results were included only if the QC values were within range. The MIC_{50}, MIC_{90}, and MIC ranges for antimicrobials for frequently tested *Chryseobacterium* species were determined. **Results:** AST was completed for 245 *Chryseobacterium* species clinical isolates, and the most frequently tested species were *C. gleum/indologenes* (n = 78), *C. hominis* (n = 25), *C. taklimakanense* (n = 14*), C. anthropi/haifense* (n = 12), *C. arthrospharae* (n = 12), *C. bernardetii/jejuense* (n = 3), *C. pallidum* (n = 3), and *C. solincola/treverense* (n = 3). 84 isolates were unable to be identified to species level, and were grouped as "*Chryseobacterium* spp." Regarding susceptibility, across all *Chryseobacterium* species, the antibiotics with the most activity included minocycline (97.8%), trimethoprim-sulfamethoxazole (TMP-SMX; 95.5%), levofloxacin (92.3%), and ciprofloxacin (82.8%). Comparing the β-lactams, piperacillin-tazobactam had the most activity (59.7%), whereas ceftazidime (42.2%), cefepime (44.3%), meropenem (41.2%), and imipenem (46.3%) had similar low activity. The highest resistance rates were found for tobramycin (96%), aztreonam (94.6%), and gentamicin (62.7%). Among the *Chryseobacterium* isolates, certain species were found to be largely pan-susceptible, including *C. anthropic/haifense*, *C. hominis*, and *C. Taklimakanense*. **Conclusions:** *Chryseobacterium* species display significant resistance against β-lactam antibiotics, which are often used for empiric therapy. Minocycline, TMP-SMX, and fluoroquinolones have the most activity against *Chryseobacterium* species clinical isolates.

Session A3: Microbiology
A14

Evaluation of the LifeScale System for Rapid Phenotypic Antimicrobial Susceptibility Testing from Positive Blood Cultures

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Objective: The spread of antimicrobial resistance is a growing threat to public health, thus there is a critical need for prompt and reliable antimicrobial susceptibility testing (AST). Rapid AST may improve patient outcomes by allowing for quicker start of optimal therapy and reducing hospital length of stay, therefore decreasing overall healthcare costs. However, rapid results may not improve patient care if they are not considered equivalent to standard AST. Several platforms are under development that can provide rapid AST results; the objective of this work is to assess the performance of the new LifeScale rapid AST platform (Affinity Biosensors) that uses resonant mass measurements for calculation of antimicrobial susceptibility results. **Methods**: Positive BACTEC blood-cultures collected from patients were included if the gram stain revealed only Gram-negative rods. Standard of care (SOC) AST results, as determined by a combination of BD Phoenix automated, Sensititre broth microdilution, and/or standard disk diffusion methods, were compared to results from direct positive blood culture testing on the LifeScale system. Minimum inhibitory concentrations (MICs) and categorical interpretations based on CLSI and/or FDA AST breakpoints were compared by microorganism and drug to calculate essential and categorical agreement for five species with pending claims on the LifeScale system: *Escherichia coli* (N=33), *Klebsiella pneumoniae* (N=10), *K. oxytoca* (N=5), *Pseudomonas aeruginosa* (N=11) and *Acinetobacter* sp. (N=1); tested against 13 relevant antibiotics: Amikacin, ampicillin, aztreonam, cefazolin, cefepime, ceftazidime, ceftazidime/avibactam ertapenem, gentamicin, levofloxacin, meropenem, piperacillin/tazobactam, and trimethoprim/sulfamethoxazole. **Results**: LifeScale had 95.3% essential agreement with the SOC results, and a 93.1% categorical agreement based on CLSI M52 criteria. Of the 665 organism-drug combinations evaluated, agreement was high, with only 1 very major discrepancy, 8 major discrepancies and 37 minor discrepancies, of which 22 (47.8%) were within ±1 doubling dilution. Among these discrepancies, LifeScale MICs averaged 1 dilution higher than SOC MICs, which may reduce the risk of false-susceptible interpretations. **Conclusions**: The accuracy and reliability of results from rapid AST is of utmost importance. The LifeScale technology is unique among AST platforms as it measures bacterial cell mass and counts to determine MICs for up to 14 antibiotics in ~4 h. These results suggest this platform is able to deliver rapid, actionable results to guide antimicrobial therapy for patients with bacteremia.

Session A4: Immunology
A15

An Unbiased Approach of Individual Tissue-specific Autoantibody Identification Using Immunoprecipitation Coupled to Mass-spectrometry (IP-MS)

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Background and aim: Autoreactive antibodies have gained increasing recognition in autoimmune diseases of the central nervous system (CNS) serving as disease drivers and / or biomarkers. Identification of novel autoantibodies therefore is crucial to optimize diagnostic work and therapy of these diseases as well as understanding their pathogenesis. Hence, we aimed to develop an unbiased strategy to identify patients' individual main autoantibodies directed against brain epitopes.
Methods: We used murine tissue-based assays to screen patients' sera and cerebrospinal fluids (CSFs) for autoreactive IgGs with known and unknown antibody targets. IgGs from autoreactive patients' samples were coupled to magnetic beads and used as a bait to pull down potential targets from homogenized brain tissue of wildtype mice. After precipitation and several washes to reduce unspecific binding, beads were subjected to on-bead tryptic digestion followed by mass spectrometry based proteomic analyses using liquid chromatography tandem mass-spectrometry (LC-MS/MS). For antibody targets identification the fold change enrichment compared to a negative control or to all other pulldown samples, as well as the protein abundance was used. Antibody target validation was done via recombinant expression of the target protein in HEK-293 cells and neutralization with the respective antigen in tissue-based immunofluorescence assays.
Results: As proof of principle, we were able to identify Grin1 Caspr2, Trim46 and Nf-h [MOU1] as main targets of patients' sera or CSF with autoimmune encephalopathy. All four antigens showed highest enrichment and/or highest protein abundance in the respective samples and have been confirmed in cell-based assays. In addition, we identified one novel anti-neuronal antibody target in serum and CSF of a patient showing a speckled staining of the granular cerebellar layer.
Preabsorbance of the serum and CSF with the recombinant protein fully neutralized the signal of the tissue-based immunofluorescence.
Conclusions: Our IP-MS approach is suitable to identify the main autoantibody targets in patients' serum and CSF within murine CNS tissue thereby providing an unbiased and scalable technique allowing for tissue-specific autoantibody determination.

Session A4: Immunology
A16

Evaluation of Different Microbead Volumes in a Single Antigen Bead Assay for HLA Antibody Detection

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OBJECTIVES: The multiplexed single antigen bead (SAB) assay is now commonly used for detection of antibodies to human leukocyte antigens (HLA) in the management of solid organ transplantation. Serum is incubated with microbeads individually coated with unique HLA antigens and the presence of antibody is detected using a secondary antibody. Due to its cost, laboratories may use a lower-than-recommended volume of reagent microbeads, although the impact of microbead volume on assay performance has not been reported. The present study seeks to determine the concordance of an SAB assay when different microbead volumes were used. Although this is also a required laboratory practice when modifications are made to an FDA-cleared assay, requirements for the validation of a multiplexed assay are currently not well-standardized. Hence, this study may also serve as an example framework for validating a clinical multiplexed assay. **METHODS**: SAB (LabScreen, One Lambda) was performed on 14 patient specimens [Mei San T1] selected to provide a range of class I and II HLA antibody levels. Each specimen was tested using three microbead volumes of 5 µL (manufacturer-recommended), 3 µL and 2.5 µL. All reactions were tested in a single session to minimize sources of variability. A mean fluorescence intensity (MFI) of ≥ 2000 was used to define positive beads, which is also the institutional threshold for defining incompatible antigens in solid organ transplantation. Concordance between different bead volumes was calculated using Cohen's Kappa. Bland-Altman plots were used to visualize bias. All analyses were performed at individual bead level. **RESULTS**: Kappa values were: 0.91 (class I) and 0.95 (class II) for 3 µL vs. 5 µL; 0.90 (class I) and 0.93 (class II) for 2.5 µL vs. 5 µL; 0.97 (class I) and 0.93 (class II) for 2.5 µL vs. 3 µL. Positive bias in MFI values was observed with lower bead volumes and was most pronounced in the 2.5 µL vs. 5 µL comparison; in contrast, MFI values between 2.5 µL and 3 µL were more similar. **CONCLUSION**: Lower-than-recommended microbead volume may be used in the SAB assay without significant impact on classification of incompatible antigens. Although positive bias in MFI values was observed with lower microbead volumes, the impact on positive vs. negative beads assignment was minimal. Since the tested microbead volumes represented 12.5-20% of the total reaction volume, such a change could have caused a matrix effect and impacted antibody-bead binding, leading to differences in MFI values. Hence, individual laboratories modifying the SAB assay should validate such modifications before implementation to ensure the accuracy of HLA antibody assignment.

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Session A4: Immunology
A17

Enhanced IgG Immune Response to COVID-19 Vaccination in Sickle Cell Disease Compared to General Outpatient Population

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Background: Adults with sickle cell disease (SCD) are considered immunocompromised due to functional asplenia, impaired humoral immunity, and susceptibility to microbial sepsis. Based on this, expert consensus guidelines have suggested that patients with SCD are at increased risk of COVID-19 infection and may warrant a distinct vaccination schedule used for immunocompromised patients. However, data specific for COVID-19 vaccination in SCD is limited and the extent to which the immunocompromised state in SCD affects vaccination response remains undetermined. **Objective:** Compare the antibody response to COVID-19 vaccination in adults with SCD to demographically matched controls. **Patients and Methods:** Following IRB approval, residual clinical serum samples from 201 adults with SCD and 201 matched non-SCD controls that received COVID-19 vaccination were collected between March to September 2022. Demographic data (age, sex, race and ethnicity), COVID-19 vaccination data (number of vaccine doses, vaccination date, and vaccine type), and SCD-related variables (sickle genotype, RBC transfusion burden, hydroxyurea, splenectomy, and number of RBC alloantibodies) were obtained from electronic health record. Serum samples were analyzed by enzyme-linked immunosorbent assay (ELISA) for IgG specific against SARS-CoV-2 receptor-binding domain (RBD) and nucleocapsid (NC). Virus neutralization activity was measured by high-throughput blockade of hACE-2 binding (BoAb) assay. **Results:** SARS-CoV-2 RBD-specific IgG level was higher in SCD vs control with median RBD-specific IgG endpoint titer of 1:54572 in SCD vs 1:31131 in controls (p = 0.0137). SCD vs control showed a similar proportion of subjects with strong (79.6% vs 78.1%), average (8.5% vs 8.0%), and weak (11.9% vs 13.9%) virus neutralization activity, respectively. There was no difference in COVID-19 natural infection rate in SCD vs control, with median NC-specific IgG endpoint titer of 835.5 in SCD vs 741.4 in control (p = 0.8779). Subgroup analysis consistently showed higher RBD-specific IgG levels in SCD vs controls across all demographic- and vaccine-related variables analyzed, though statistical significance (P ≤ 0.05) was observed only for the following subgroup comparisons: female, Black or African American, 2 doses of COVID-19 vaccine, and >365 days since last vaccine dose. No difference in IgG level was detected by subgroup analysis across SCD-specific variables as defined above. **Conclusions and Relevance:** These data suggest that patients with SCD, despite their immunocompromised state, generate a more robust and durable IgG response to COVID vaccines compared to the general population, with similar prevalence of strong neutralizing antibodies. Consistent trend across demographic-, vaccine-, and SCD-related variables analyzed suggest that the same COVID-19 vaccination regimen as the general population will confer a similar immune response in patients with SCD. Combining high-throughput serosurvey of residual clinical samples with electronic health record data extraction may be a useful approach to evaluate humoral responses after vaccination against other highly pathogenic agents in patients with SCD.

Session A4: Immunology
A18

Observations from Mass-Fix: Prevalence and Characteristics of Therapeutic Monoclonal Antibodies (t-mabs) Detected by Isotyping of Monoclonal Immunoglobulins via MALDI-TOF Mass Spectrometry

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Matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry ("Mass-Fix") has replaced serum immunofixation at our institution for detection of monoclonal immunoglobulins. One advantage of Mass-Fix is the ability to differentiate pathogenic endogenous monoclonal antibodies from therapeutic monoclonal antibodies (t-mabs), which are often the first-line treatment for multiple myeloma, by reviewing the light chain signature mass. The objective of this study was to describe the distribution of t-mabs and other key characteristics of clinical serum samples analyzed by Mass-Fix in 2022. Comprehensive results for each sample were extracted retrospectively from the laboratory information system. Of 66,710 total analyzed, 30,701 (46%) samples were reported as "positive" (i.e., contains a monoclonal protein), given the tertiary nature of our institution and reference laboratory services. The positive samples were further subdivided by t-mab (detected by Mass-Fix), with a total of 7,769 (25.3%) t-mabs reported. The top five IgG kappa t-mabs reported include daratumumab (n=6,537), elotuzumab or REGN5458/5459 (n=499), isatuximab (n=348), and rituximab (n=102). Rare observations included monoclonal proteins consistent with tixagevimab/cilgavimab, for COVID-19 infection (n=7), obinutuzumab, an anti-CD20 t-mab for multiple sclerosis (n=1) and evolocumab, an IgG lambda anti-PCSK9 inhibitor (n=6). Of the 7,769 samples, the t-mab was the only reported clone in 47.7% of cases and was found along with the original disease-associated clone in remaining cases. When the original disease clone was present, it was an IgG kappa isotype 31% of the time and could have confounded the definition of complete therapy response for patients. 69% were non-IgG kappa original clones. Mass-Fix test orders have a multiple-choice prompt to provide any current therapy to aid in the patient's result interpretation. For those samples where a t-mab was reported, the answer to this question regarding administered therapy was often discrepant from the report: only 38.5% of daratumumab-positive samples had an affirmation of daratumumab administration. The remaining 61.5% of daratumumab-positive samples reported an assortment of therapies, including bone marrow transplant, other t-mabs, no active therapy, or the field was left blank, highlighting poor compliance. Additionally, 154/36,009 samples where the provider affirmed daratumumab administration were reported as negative (i.e., no monoclonal protein observed on Mass-Fix). Often, the send-out laboratory does not have medical record access where treatment information is detailed. In conclusion, we reported the presence of a t-mab in 11.6% of all samples tested with Mass-Fix, suggesting that t-mabs have entered the clinical practice to stay, and accurately determining their presence in the challenging environment of poor compliance to prompt questions and evolving treatment regimens is something that cannot be ignored by clinical laboratories. Mass-Fix allows detection of a t-mab in the same routine run as other testing, without need of a second immunofixation to rule out the IgG kappa finding is not a t-mab.

Session A5: Hemoglobin and Troponin Testing
A19

Impact of Implementing Point of Care Hemoglobin A1C Testing in an Obstetrics Outpatient Clinic

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Hemoglobin A1C ≥ 6.0% is associated with increased risk of adverse outcomes in pregnant, diabetic patients and is recommended as a secondary measure of glycemic control in pregnant patients by the American Diabetes Association. However, the utility of A1C point of care testing (POCT) during pregnancy to facilitate rapid counseling and diabetes care, particularly in relatively low-income transient patient populations is unknown. We performed a single center, retrospective analysis of patients presenting to an out-patient obstetrics office with routine, In-lab A1C (n= 70) testing and after the implementation of POCT for A1C (n=75). Demographics, results, physician referral to a nutritionist, counseling, and outcomes were retrieved from the electronic medical record. 9% and 23% of the In-lab group and POCT respectively were referred for nutrition services (p=0.02). 22% of the In-lab group and 42% of the POCT groups received immediate counseling (p<0.01). An inverse correlation was observed between entry A1C and the weeks at delivery with a Pearson r of -0.39 (-0.58-0.16) for the In-lab group and -0.38 (-0.57--0.14) for the POCT group. In conclusion, the implementation of POC A1C testing was associated with immediate counseling and management of pregnant patients.

Session A5: Hemoglobin and Troponin Testing
A20

Resolving the Impact of hs-Troponin I Carryover on Beckman Coulter Access DXI 800 in Academic Hospital Settings

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The high-sensitivity cardiac troponin (hs-TnI) assays are deemed as the preferred biomarker for diagnosing myocardial injuries. However, the hs-TnI test is not perfect, and one of the most common drawbacks is carryover. The consequences of carryover can be severe, leading to misdiagnosis, unnecessary and costly interventions, and additional anxiety and stress for the patient mentally and financially. Additionally, carryover causes extended instrumentation downtime and potential delays for result turnaround time. During method implementation phase, the carryover issue was brought up by the clinical laboratory scientists and, subsequently, by the vendor (Beckman Coulter). In a setting of our laboratory, the carryover presents at a far lower concentration than the manufacture's claims. In order to address the issue, Troponin carryover protocol was designed and optimized to identify and mitigate contamination as well as to minimize impact on laboratory operations. The protocol is automatically activated for all samples with a concentration higher than the upper limit of linearity of 25,000 ng/L. After the initiation of the protocol, the instrumentation downtime and reagent waste significantly dropped by 75%. There was little interruption to turnaround time, and the entire process freed up many resources for patient care improvement. Although the root cause of carryover in hs-TnI remains unknown, the awareness of the issue alerts the clinicians and laboratorians when suspicious elevated hs-TnI results occur. This study provides a valuable and thorough guide to minimize the carryover impact in hs-TnI assay and to optimize testing workflow.

Session A5: Hemoglobin and Troponin Testing
A21

Comparability of Beckman Coulter Access Cardiac Troponin I Assays

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Cardiac troponins (cTn) are the most sensitive and specific biomarkers of myocardial injury. The rise and/or fall of cardiac troponins above the 99th percentile of the upper reference limit (URL) is required in the assessment of acute myocardial infarction. In our institution, high sensitivity troponin I (hsTnI) is performed on four Access 2 Immunoassay Systems and three DXI 800 Access Immunoassay Systems. As a regional medical center, we accept patients from outside hospitals where contemporary cardiac troponin I (cTnI) were performed. The results from different assays and platforms may disagree and lead to incorrect explanation of the results as false rise and/or fall of cTn. To harmonize results among these assays, we analyzed the variation between the two assays of cTnI and hsTnI, and the concordance of same assay hsTnI on different instruments using patient specimens. To investigate the between-method variance, 424 patient specimens with troponin levels ranging from 0-23370 ng/L were used to measure both cTnI and hsTnI on DXI 800 instruments. To investigate the within-method agreement, 43 patient specimens with troponin levels ranging from 2-114394 ng/L were used to measure hsTnI on Access 2 and DXI instruments. The between-method comparison of cTnI and hsTnI on DXI showed a slope of 1.003 with intercept of -43.31 and correlation coefficient (CC) of 0.9590. The mean bias was -5.1%, which was within the analytical imprecision range determined in our laboratory (2.2%-10.7%). However, comparison of cTnI and hsTnI in patients with troponin <20ng/L (n=103), the 99th percentile of the URL for males, showed the slope was 1.325 with intercept of -0.97 and CC of 0.7462. The mean bias was 1.91 (21.53%), which was much larger than the analytical imprecision. This is consistent with the fact that cTnI results are not reliable at the lower level due to the imprecision problem. Comparison of cTnI and hsTnI in patients with troponin >20ng/L (n=321) showed the slope was 1.006 with intercept of –60.09 and CC of 0.9576. The mean bias was -54.30 (-5.23%), which was within the analytical imprecision range. The within-method comparison of hsTnI on Access 2 and DXI 800 showed the slope was 1.138 with intercept of -633.0 and CC of 0.9888. The mean bias was 2126.4 (10.6%), within the analytical imprecision range. These data indicate that cTnI results above the 99th percentile URL are comparable with hsTnI results if both are tested on DXI 800, and hsTnI results tested on Access 2 and DXI 800 are comparable. Thus, to use the cardiac troponins assay properly, we suggest the laboratory report cardiac troponins with the assay and instrument names to reduce confusion during results comparison.

Session A5: Hemoglobin and Troponin Testing
A22

Hemoglobin A1c Control is an Independent Predictor of Circulating Troponin Concentrations Using Machine Learning

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Diabetes mellitus (DM) is associated with multiple comorbidities that may precipitate cardiac damage and elevated cardiac troponin (cTn) concentrations including renal failure, hyperlipidemia (HLD), hypertension (HTN), coronary artery disease (CAD), and congestive heart failure (CHF). Diabetics >70 years old have a higher likelihood of adverse outcomes including major cardiovascular events and cardiac mortality. However, the risk to younger diabetic patients and the precipitating factor(s) that facilitate cardiac injury in those with DM are unknown. The objective of this study was to investigate factors predictive of cTn concentrations in young, relatively healthy diabetic patients. We collected 1,533 remnant plasma samples from outpatients between 06/22-09/22 with physician ordered hemoglobin A1c testing. cTn was measured using the Abbott ARCHITECT High Sensitivity Troponin-I assay (limit of detection = 1.7 ng/L, imprecision = 4.76% at 50 ng/L). Demographic information (sex, race, BMI) and pertinent medical history (diabetes, HTN, HLD, CAD, CHF) were collected from the electronic medical record, along with estimated glomerular filtration rate (eGFR) and hemoglobin A1c. Exclusion criteria included: patients with missing laboratory data, those undergoing cancer treatment, or a history of myocardial infarction/cardiomyopathy/cardiac surgery. Troponin results were classified as normal- or high-risk using a cut-off of 10 ng/L for females and 12 ng/L for males, thresholds previously shown to correlate with incidence of cardiovascular disease risk within 15 years. Univariate statistics were calculated using bootstrap resampling. An XGBoost model was trained to predict high-risk troponinemia, and summary statistics were calculated on a held-out test set. Of the 1,135 patients that met inclusion criteria, 621 (54.7%) were female. The median age was 60 years (IQR: 49-69 years) and the median A1c was 6.2% (IQR: 5.8-7.0%). A total of 746 patients (65.7%) had a prior diabetes diagnosis, with 156 patients (13.7%) having prediabetes, 42 patients (3.7%) having Type 1, and 548 patients (48.3%) having Type 2. Median troponin concentration for patients with an A1c <5.7% was 1.6 ng/L (IQR: 0.8-3.4), 5.7-6.4% was 2.2 ng/L (IQR:1.3-4.8), and ≥6.5% was 2.9 ng/L (IQR: 1.6-6.7). Univariate analysis demonstrated significant differences in troponinemia by age (CI of difference: 4.4-8.9 years), A1c (0.2-0.7%), and eGFR (28-38mL/min/1.73m^2). The machine learning model demonstrated strong predictive capacity (sensitivity: 0.74, specificity: 0.86, PPV: 0.5, NPV: 0.92, area under ROC curve: 0.91). The features with the greatest impact on area under the ROC curve when removed were eGFR, Age, A1c, and CHF, suggesting a combination of clinical and laboratory variables can be used to predict circulating troponin concentrations in outpatients. Results of both univariate and multivariate analyses suggest that A1c control is an independent contributor to cTn concentrations. Ultimately, this study provides evidence that glucose control may be associated with cardiac damage and future cardiovascular events, warranting longitudinal outcome studies.

Session B1: Young Investigator Award with Distinction
B01

Development of a Machine Learning Decision Support System for Clinical Flow Cytometry

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High parameter flow cytometry is a highly utilized tool in both research and clinical settings for accurate immunophenotyping in immunology, oncology, and many other disciplines. With increasing dimensionality, manual analysis of data becomes more complex and time consuming. Over the past decade, several automated methods have been developed for cell population clustering and dimensionality reduction of high parameter flow cytometry data which have sped up and simplified the discovery of cell populations not observed by manual gating strategies. However, the input and output of such tools are stochastic in nature, thus making their results difficult to reuse with novel samples such as diagnostic patient samples. Several groups have recently attempted to utilize machine learning algorithms to analyze clinical flow cytometry data. These studies focused on training machine learning models with a goal of predicting a specific diagnosis for each sample. This approach can be limiting when the diagnostic features are not perfectly met to predict a specific diagnosis as well as the absence of the patient's clinical data. To our knowledge, no studies have utilized machine learning to identify and classify individual cells based on their raw fluorescence signature to various cellular populations, whether normal or abnormal, to aid a diagnostician to interpret their significance in a clinical context. In this study, we utilized a data set of ~240 million individual cells from ~9,500 flow cytometry files from 2,300 patients to train a machine learning model to predict cell population classifications as annotated by expert hematopathologists. These annotations were implemented into an end-to-end machine learning based decision support system allowing for rapid, automated analysis of high dimensional flow cytometry data with an output aiding the diagnostician in the generation of a diagnosis. A clinical validation highlighted the robustness of this methodology with 100% sensitivity and 94% specificity in the identification of abnormal B-cell populations on a cohort of 1,500 patients. This decision support system also identifies abnormal T-cell and myeloid cell populations with 100% sensitivity. Overall, the decision support system saves significant time as it removes the need for manual gating and analysis, and aids the diagnostician in identifying discrete cell populations and offering descriptive information about any abnormal populations identified.

Session B1: Young Investigator Award with Distinction
B02

Automated Machine Learning-Based Diagnosis and Molecular Characterization of Acute Leukemias Using Flow Cytometry Data

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Current flow cytometric analysis of blood and bone marrow samples for the diagnosis of acute leukemias relies heavily on manual intervention in both the processing and analysis steps, introducing significant subjectivity into the resulting diagnosis and increasing diagnostic turn-around time. Additionally, concurrent molecular characterization of these samples via cytogenetics and targeted sequencing panels can take multiple days, thereby delaying patient diagnosis and treatment. Attention-based multi-instance learning models are machine learning models that can make accurate predictions and generate interpretable insights regarding the classification of a sample from multiple events/cells; while these models have been developed for anatomic pathology applications, they have yet to be applied to flow cytometry data. By utilizing 1,820 flow cytometry samples from 2019-2022 at Brigham and Women's Hospital, we developed attention-based multi-instance machine learning models for automated diagnosis of acute leukemia, including differentiation of acute myeloid leukemia (AML) from B-lymphoblastic leukemia/lymphoma (B-ALL). Additionally, using concurrent cytogenetic and targeted sequencing data from 674 acute leukemia samples, machine learning models for prediction of molecular aberrancies from flow cytometry data were developed. Machine learning models were created using the TabNet deep learning architecture and VIME self-supervised training algorithm, which are state-of-the-art approaches towards machine learning from tabular data including flow cytometry data. Attention-based multi-instance models demonstrated strong performance for the automated diagnosis of acute leukemia versus non-leukemia samples (AUROC 0.869), as well as the separation of AML from B-ALL samples (AUROC 0.971). These models also accurately predicted cytogenetic aberrancies among AML samples, including t(15;17);*PML::RARA* (AUROC 1.00), as well as mutations including *NPM1* (AUROC 0.725). These models do not require any manual intervention including compensation or gating, and additionally provide quantitative scores for the relative importance of different flow cytometry events and markers for the diagnosis of a particular sample. These importance scores can be integrated into flow cytometry analysis software for visualization and interpretation by hematopathologists. In this study, we have demonstrated the capability of machine learning models to provide automated diagnoses of acute leukemia, as well as accurately predict cytogenetic and molecular aberrancies in blood and bone marrow samples using flow cytometry data. This automated workflow can significantly decrease diagnostic turn-around time and ultimately improve patient outcomes.

Session B1: Young Investigator Award with Distinction
B03

POT1b Represses ATR DNA Damage Response at Telomeres

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A complex of six proteins, known as the shelterin complex, protects telomeres from inappropriately activating a DNA damage response (DDR). Protection of Telomeres 1 (POT1) is the only member of the shelterin complex that binds single-stranded telomeric DNA through two oligosaccharide-oligonucleotide binding (OB) folds in its N-terminus. Single-stranded DNA can be bound by replication protein A (RPA) which activates the ATM-telangiectasia and Rad3 related (ATR) DDR pathway. POT1 binding to telomeres blocks RPA access to telomeres, preventing activation of an ATR-dependent DDR. Several cancer-associated mutations have been reported in the OB-folds of human POT1 that are known to cause telomere dysfunction and genomic instability. Mice possess two functionally distinct POT1 proteins, POT1a and POT1b. Previous investigations have found that only POT1a but not POT1b is required to repress ATR pathway activation. Given the high degree of homology between these two proteins, it remains unclear why POT1b cannot repress the ATR pathway as its ability to bind telomeric DNA *in vitro* is indistinguishable to POT1a. In this study, we discovered that extensive passaging of $Pot1b^{-/-}$, SV-40 immortalized mouse embryonic fibroblasts in SCID mice led to the generation of dysfunctional telomeres. DNA damage was detected using immunofluorescence-FISH to detect γ-H2AX, a marker of DNA damage, and telomere FISH foci colocalization termed telomere dysfunction induced foci (TIFs). Consistent with previous findings, we found no TIFs in early-passage $Pot1b^{-/-}$ nor late-passage $Pot1b^{+/-}$ cells. However, 18% of nuclei in late-passage $Pot1b^{-/-}$ cells contained ≥5 TIFs. These findings suggest that POT1b does possess telomere end-protection functions. We confirmed this hypothesis by showing that POT1b but not POT1a overexpression repressed TIF formation. Reconstitution with POT1a and POT1b domain-swapped mutants revealed that TIF repression is contained in the N-terminus OB-folds of POT1b. Treatment with an ATR inhibitor abolished TIF formation, implicating activation of the ATR pathway in $Pot1b^{-/-}$ cells. Furthermore, we found that overexpression of human POT1 in late-passage $Pot1b^{-/-}$ cells repressed TIF formation. Our findings confirm that POT1a and POT1b are both *bona fide* repressors of the ATR pathway. However, each protein protects telomeres through a unique pathway and loss of either POT1 protein cannot be substituted by the other. Our data suggests that specificity of end-protection unique to each POT1 protein is contained in its OB-folds. Our data provides mechanistic insight into how human POT1 protects telomere ends from activating a DDR to initiate tumorigenesis.

Session B1: Young Investigator Award with Distinction
B04

Role of T Cell Immunosenescense in Modulating Gut Microbiome

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Though the effect of the microbiome on influencing homeostasis of the immune system is well documented fewer studies have evaluated the effect of the immune system on microbiome distribution. Though adaptive host IgA responses have been shown to strongly influence the local microbiome, the systemic effects of T cells in shaping the gut microbiome have not been previously evaluated. To evaluate the systemic effects of T cells on the gut microbiome, we used data from 50 healthy volunteers aged 50-75 years, who were enrolled in a double-blinded, randomized placebo-controlled pilot trial and received a standard dose of aspirin (325 mg, N = 30) or placebo (N = 20) once daily for 6 weeks (ClinicalTrials.gov NCT02761486). Eleven T-cell subsets were measured at baseline using immunophenotyping and gut microbiome was measured at baseline and after 6 weeks of follow-up using 16s rRNA sequencing. The microbial genera and T-cell subsets were log-transformed to approximate normal distribution. We performed all the analyses separately for the baseline (cross-sectional) and longitudinal change in general after the 6 weeks. We used an unsupervised sparse canonical correlation analysis (sCCA) to generate canonical factors that explain the multi-dimensional correlation between microbiome and T cell subsets. Then we performed multivariable linear regression models to evaluate the association between selected T-cell subsets and microbiome after adjusting for age, sex, body mass index (BMI), and treatment (aspirin/placebo). In the cross-sectional analysis, percentages of naïve T cells were positively associated with the relative abundance of Intestinimonas and Sporobacter, whereas the memory T cells were inversely associated with Intestinimonas and positively associated with Dorea. In the longitudinal analysis, the baseline percentage of naïve T cells was positively associated with the change in the relative abundance of Intestinimonas, Sporobacter, Pseudobutyrivibrio, and inversely associated with Faecalibacterium. The baseline percentage of memory T cells was positively associated with the change in Dorea, Faecalibacterium and inversely associated with Intestinimonas, Sporobacter, Pseudobutyrivibrio, Streptococcus, and Flavonifractor. Notably, all the bacterial genera that were associated with baseline T cell subsets belonged to the bacterial phylum Firmicutes. Previous studies showed that the bacteria in Firmicutes phylum contribute to the production of butyrate and other short-chain fatty acids (SCFAs) and are essential to maintain gut homeostasis. This is the first study evaluating the association between T cell subsets and changes in the gut microbiome in healthy participants. Our study demonstrates that the T cell profile influences the microbiome taxa among healthy individuals. The findings from our study can pave way for future experimental studies focusing on the role of T cell immunosenescence in impacting gut microbiome and thereby maintaining gut homeostasis.

Session B1: Young Investigator Award with Distinction
B05

Comparison of Two Free Light Chain Assays: Performance of the Free Light Chain Ratio as Risk Factor for MGUS Progression

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Monoclonal gammopathy of undetermined significance (MGUS) is the most common plasma cell dyscrasia, present in ~3% of the population over 50yo. MGUS carries a 1% per year risk of malignant transformation for the rest of the affected individual's life; long-term followup is recommended for all patients with MGUS. Different risk stratification models exist to evaluate potential for progression to malignancy. The Mayo risk model, published in 2005, uses the presence of 3 risk factors (abnormal free light chain (FLC) kappa/lambda ratio (KLr), M-spike ≥1.5 g/dL, non-IgG isotype) to confer a 3% per year risk of progression instead of the average 1%. For many years, the only FDA-approved measurement of FLC was the FreeLite assay (Binding Site), which uses polyclonal sheep antibodies. Recently, other FLC assays have become available in the US, including the Sebia FLC ELISA, which employs rabbit polyclonal antibodies. The assays have similar reference intervals (RI), however differences in analytical performance between the FreeLite and Sebia were previously reported. The objective of this study was to determine the performance of the Sebia FLC assay in the Mayo risk stratification model of MGUS patients for progression in comparison to FreeLite. Cryopreserved serum samples from a cohort of 923 MGUS patients with available long-term clinical followup (median follow-up time: 7.7years, range: 0.0 to 46.9) was used to measure FLC using Sebia ELISA on a DS2 automated platform (Dynex) and FreeLite on a Siemens BNII nephelometer. Passing-Bablok (P-B) regression and Spearman correlation were used to compare the KLr between assays. Cox proportional hazards models for progression to multiple myeloma or a related plasma cell malignancy were used to estimate the prognostic effect and ability to discriminate low and high risk of abnormal KLr for each assay. Analyses were carried out in R software. Correlation between Sebia and FreeLite KLr had a Spearman r = 0.796; P-B fit: Sebia KLr = 0.825*(FreeLite KLr) – 0.048, 95% CI of slope: 0.810-0.839). With FreeLite, 32.9% of patients had a KLr outside RI for the method. For Sebia, 48.0% of patients had a KLr outside the method specific RI. Despite the individual samples analytical disagreement, both assays showed similar clinical performance for risk stratification: Sebia abnormal KLr was associated with a hazard ratio (HR) of 2.77 (95%CI: 1.79-4.28 c-statistic=0.6505) for progression, while FreeLite abnormal KLr was associated with a HR of 3.31 (95%CI: 2.20-5.00, c-statistic=0.6529), and the difference in c-statistics was not statistically significant (p=0.93). The risk assessment is performed only once per patient, at the initial diagnosis of MGUS. The similarity in clinical performance between FreeLite and Sebia assays support the use of either method as a predictor for risk of progression for MGUS patients.

Session B1: Young Investigator Award with Distinction
B06

Identification of Extracellular Vesicle-based Protein Markers of Disease Pathology in Alzheimer's Disease

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Background: Alzheimer's disease (AD) is a progressive and fatal neurodegenerative disorder which begins years before the emergence of classical symptoms such as impaired memory and cognition. Currently available diagnostic tools are unable to detect the disease prior to symptom onset and thus limit the potential for early intervention, risk stratification and monitoring of response to therapy. Extracellular vesicles (EVs) have recently been implicated in neurodegenerative diseases as a potential propagation mechanism for protein aggregates and have shown promise as peripheral matrix for markers of disease burden. Accordingly, the objective of this study was to investigate EV based protein biomarkers of disease pathology in AD using an untargeted differential proteomics approach. **Methodology**: Residual frozen CSF samples were obtained from 20 individuals undergoing evaluation for AD. Patients with pathological changes associated with AD were defined by measured phosphorylated Tau (pTau181)/amyloid β(1-42) (Aβ42) CSF ratio (pTau181/Aβ42 ratio) of >0.023 (cases: n=10, mean=0.086 ± 0.038 SD; controls: n=10, mean=0.009 ± 0.002 SD). Large and small EV populations (LEVs, SEVs, respectively) were isolated from 1.0ml of CSF using size exclusion chromatography followed by ultracentrifugation. Isolated EVs were digested with trypsin and analyzed by nano liquid chromatography coupled to tandem mass spectrometry (nano-LC-MS/MS) on a tribrid orbitrap mass spectrometer with a label free proteomics workflow. Raw data files were searched with MaxQuant and protein intensities were log2 transformed for differential expression analysis. **Results**: Proteomics analysis identified 1130 and 669 different proteins in the SEV and LEV fractions respectively after common contaminants were filtered. Several accepted EV markers, including CD9, CD81, and PDCD6IP were among the identified proteins indicating the presence of bona fide EVs. Using a criterion of Benjamini-Hochberg FDR adjusted p-value ≤ 0.05 and a log2 fold change ≥ ±1.0, 7 and 16 proteins were significantly differentially expressed in the SEV and LEV fractions respectively. Several proteins found to be upregulated in the SEV and LEV fractions, including HTRA1(SEV log2FC=1.94, p=0.005), OLFML3 (LEV log2FC=2.3, p=0.017), and NELL2 (LEV log2FC =1.91, p =0.017) have previously been implicated in AD and are among the most highly upregulated proteins in amyloid plaques. Further, several proteins not previously implicated in AD, including POMGNT1 which was upregulated in both EV fractions (SEV log2FC=3.1, p=0.037;LEV log2FC=4.2, p<0.001), were also found to be regulated in the AD cases. **Conclusion**: This study demonstrates that SEC based isolation followed by nano-LC-MS/MS allows for deep and quantitative CSF derived EV proteome comparisons. Using this approach, several promising candidate EV based markers of AD pathology were identified. Of these, several proteins including HTRA1, OLFML3, NELL2 have previously been implicated in AD and are known to be expressed in the brain, warranting further investigation as potential peripheral markers of AD pathology.

Session B2: Chemistry
B07

LC/MS-MS Quantification of Myo-inositol: A Novel Biomarker for Kidney Disease

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Creatinine is the primary biomarker used for assessing kidney function in patients with suspected acute and chronic kidney injury. However, creatinine, a product of muscle creatine metabolism, is an imperfect proxy for renal function because it is subject to non-renal interferences including muscle mass, diet, and medications. Creatinine is particularly problematic as a biomarker of acute kidney injury (AKI) due to relatively high renal function reserve, requiring considerable kidney damage and time for a clinically significant change in creatinine to be detected. Given that AKI and chronic kidney injury (CKD) are associated with high mortality, morbidity, and contribute significantly to health care costs, there is an unmet need for highly sensitive and specific biomarkers for assessing renal function in patients.

Myo-inositol oxygenase (MIOX) is a novel biomarker limitedly expressed in the proximal renal tubules. MIOX concentrations are elevated in mice with renal injury and in critically ill patients with AKI. Our previously published studies have demonstrated that elevation in MIOX concentrations precedes changes in creatinine concentrations by approximately 54 hours. Importantly, MIOX facilitates the conversion of myo-inositol to glucuronic acid.

We developed a robust LC-MS/MS method to quantify myo-inositol in human plasma, hypothesizing that following renal injury (acute and chronic), plasma concentrations of myo-inositol will increase, and will correlate with increases in serum creatinine concentrations. A healthy outpatient cohort was identified from samples obtained from out-patients with normal plasma creatinine, eGFR>60, as well as normal urine protein: creatinine ratio, albumin: creatinine ratio, or urinalysis results that were pan-negative/pan-normal. Remnant samples from out-patients with clinically staged CKD who have not initiated dialyses were selected for the CKD group.

In healthy adult out-patients with stable renal function, the central 95th% distribution of plasma myo-inositol concentrations was 16.61 - 44.2 uM (Median 27.7uM, 95% CI: 26.7-28-7). No sex-based differences in plasma myo-inositol were observed. We also observed excellent correlation between plasma myo-inositol and serum creatinine concentrations (r=0.84, 95% CI: 80-88), as well as excellent sensitivity (99%) and specificity (100%) at a myo-inositol concentration of 50.22uM for differentiating patients with stable kidney function from those with CKD. Patients with CKD exhibited higher plasma myo-inositol concentrations (p value <0.0001) with a central 95% percentile of 51.2-309.1 uM (Median 104.1 uM, 95% CI: 92.3- 113.6).

These results imply that *myo-inositol concentrations increase in accord with renal injury and MIOX buildup in patients with kidney dysfunction, making it a potential biomarker for renal impairment*.

Session B2: Chemistry
B08

Alternative Strategies to Provide Actionable Results When Supply of Urinalysis Strips Is Unavailable

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Urinalysis “dip strips” offer physicians qualitative results of 6 analytes which are immediately actionable: protein, glucose, leukocyte esterase, nitrates, blood, and ketones; however, the strips are instrument specific such that they are at the mercy of supply chain shortages. Due to vendor supply issues, we implemented a strategy that would continue to support clinical decision making in the absence of supplies for protein, glucose, white blood cells (WBC) and blood (RBC) detection. Method: In supply shortage situations, an automated algorithm triggered such that urine samples would be sent to the automation chemistry line to run quantification of protein and glucose and make sure an automated urine microscopy was performed for RBC and WBC detection. The algorithm triggered printing two labels so nursing would collect two specimens. We monitored the turn-around time from the specimen being received in the laboratory to results, made sure that the culture reflex order was triggered, and tracked complaints by physicians regarding not having all usual urinalysis results provided by the strips. Prior to implementation, correlation between sample types for protein and glucose measurement was found acceptable. RESULTS: When we put in place the algorithm, the turn-around time of urine microscopic study was identical to that obtained when the urinalysis was done with the strips; however, the quantification of glucose and protein took approximately 30 minutes more. Urine reflex cultures were triggered correctly with the algorithm as they derive entirely from a WBC count >20. During the period we had the algorithm in place we only had one complaint by a physician wanting to have results of nitrates. Conclusion: The successful implementation of the algorithm allowed the laboratory to provide actionable urinalysis analytes in a timely manner with minimal complaints from physicians.

Session B2: Chemistry
B09

Assessing the Reliability of Creatinine-Estimated Glomerular Filtration Rate in Living Kidney Donor Candidates: Does It Measure Up to the Measured Rate?

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A living donor kidney transplant is the best therapy option for patients with end stage renal disease (ESRD); however, it is associated with an increased risk of ESRD development in the donor. Thorough evaluation of the donor candidate’s kidney function status is essential for the appropriate selection of candidates with minimal risk of post-donation kidney dysfunction.
In this study, glomerular filtration rate (GFR) values measured by iohexol plasma clearance (mGFR) and estimated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-Epi) creatinine equations (eGFR), with and without the race factor (2009 and 2021 CKD-Epi equations, respectively), were compared in a cohort of 303 kidney donor candidates. GFR values were analyzed using Bland-Altman plots, linear regression, Mann-Whitney U tests, and p10 and p30 values.
Bland-Altman analysis revealed a lack of agreement between the 2009 and 2021 CKD-Epi eGFR and corresponding mGFR values, with both equations showing a negative bias of 10 – 11 mL/min/1.73 m2 and indicating an underestimation of creatinine-eGFR. eGFR underestimation was confirmed by Mann-Whitney U analysis; median GFR values were significantly lower for both CKD-Epi equations as compared to corresponding iohexol-measured values (2009: 85.86; 2021: 87.29; mGFR: 96.58). Despite the overall underestimation, over 14% of donor candidates with eGFR >90 mL/min/1.73 m2 had an mGFR value <90 mL/min/1.73 m2. Conversely, 36% - 38% of donors with normal kidney function of >90 mL/min/1.73 m2 as determined by iohexol-mGFR had corresponding eGFR values <90 mL/min/1.73 m2. eGFR showed a significant but poor correlation with mGFR, with R2 values of 0.2775 and 0.2803, respectively. While the 2021 eGFR equation had better accuracy as compared to the 2009 equation (p30 of 81% versus 76%), it displayed low overall accuracy with a p10 of <43%. Separate analysis of Black donor candidates’ eGFR and mGFR values revealed similar trends as observed for the total cohort. While exclusion of the race factor in the 2021 CKD-Epi equation slightly improved accuracy (p30 of 77% versus 72%), the correlation with mGFR remained poor for both equations (R2: 0.1455 and 0.1377 for the 2009 and 2021 equations, respectively).
The results of this study confirmed that creatinine-eGFR values, regardless of the race factor, differ significantly from iohexol-mGFR. Our data shows that even potential kidney donors with eGFR >90 mL/min/1.73 m2 cannot be presumed to have normal kidney function, while eGFR <90 mL/min/1.73 m2 cannot accurately exclude donor candidates. We conclude that creatinine-eGFR cannot reliably serve as a substitute for mGFR in the context of living donor kidney function evaluation.

Session B2: Chemistry
B10

Analytical Performance Evaluation of BioRad's Unassayed Multiqual, Immunoassay Plus and Assayed Multiqual InteliQ Tube-Based Quality Control Materials

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Introduction: Quality control (QC) practices commonly require aliquoting of liquid material into sample cups prior to analysis. Recently, newer tube-based QC has become available that can be scanned directly onto the analyzer without additional aliquoting. In this study, we evaluate the performance of the BioRad's Unassayed Multiqual (Mutiqual), Immunoassay (IA) Plus and Assayed InteliQ Muliqual (InteliQ) tube-based QC material.
Materials and Methods: The analytical performance of Multiqual, IA Plus and InteliQ materials were compared over 14 days at three concentrations on an Abbott Alinity ci analyzer system. The analysis included 20 unique clinical chemistry and 4 immunoassay analytes. For an applied comparison, all QC materials were analyzed using the same lot on multiple days, times, and by various laboratory team members (n=10). The means, standard deviations (SD) and coefficient of variation (CV) were calculated for each analyte. Minimum acceptable allowable imprecision (I) specifications were set using the biological variation (BV) database from European Federation for Laboratory Medicine (EFLM), which was calculated for each analyte using the equation I = 0.75*CV within-subject. Sample cups used for Multiqual and IA plus were also calculated to determine consumable waste for these materials over the study period and extrapolated for a year.
Results: Multiqual, IA Plus and InteliQ CVs for each analyte were compared to the EFLM BV database and showed comparable results for most analytes studied. Most analytes demonstrated < 5% CV over the 14-day period for InteliQ except alkaline phosphatase, bicarbonate, total bilirubin, and triiodothyronine for either 1, 2 or 3 levels. Total bilirubin and free thyroxine were outside this CV for Multiqual and IA Plus. In addition, minimum acceptable allowable imprecision goals from EFLM were not met for several analytes that were included in InteliQ such as albumin, alkaline phosphatase, aspartate aminotransferase, calcium, bicarbonate, chloride, and sodium. Multiqual and IA plus analytes that did not meet imprecision goals were bicarbonate, chloride, sodium, and free thyroxine, respectively. A total of 84 sample cups were needed to perform Multiqual and IA plus QC analysis over the study period or approximately 2184 over a year.
Conclusion: Multiqual, IA Plus and InteliQ QC materials provide similar analytical performance although each material had some analytes that did not meet acceptable imprecision limits defined by EFLM. Implementation of new tube-based QC materials can reduce sample cup consumables and may reduce technologist time required to aliquot Multiqual and IA Plus.

Session B2: Chemistry
B11

Rapid Resolution of Medically Relevant Polyunsaturated, Very Long-, Odd-, and Branched-Chain Fatty Acid Methyl Esters

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Fatty acids play an important role in human health and disease. Nearly 100 years ago, the Burrs demonstrated that polyunsaturated fatty acids (PUFAs) were essential for development; subsequent work uncovered the role of PUFAs as precursors to important signaling molecules such as prostaglandins, leukotrienes, and thromboxanes. Very long chain fatty acids (VLCFAs) originally sparked interest over 40 years ago for being elevated in humans with peroxisomal disorders. More recent studies have shown that VLCFAs are elevated in healthy human controls, compared to their diabetic counterparts. In a similar vein, odd chain fatty acids (OCFAs) and branched-chain fatty acids (BCFAs) of the iso and anteiso variety are higher in humans with insulin sensitivity than in insulin resistant individuals. These families of fatty acids are most frequently analyzed as their fatty acid methyl esters (FAMEs) by gas chromatography (GC). Regrettably, even recently published methods resolving BCFAs from their linear correlates have run-times in excess of an hour and, in some cases, over 100 minutes.
Objective: The goal of this study was to decrease the GC run-time for the analysis of FAMEs relevant to human health and disease.
Methods: Baseline resolution of FAMEs required careful combination of the right gas chromatograph, column dimensions, stationary phase, carrier gas, and temperature programming.
Results: We cleanly resolved the FAMEs of all common polyunsaturated, very long-, odd-, and branched-chain fatty acids with baseline separation in only ~15 minutes – a 4-fold improvement over many existing methods.
Conclusion: This method will significantly improve analysis of fatty acids in health and disease, especially in large-scale, clinical studies, by quartering the run time necessary to resolve PUFAs, VLCFAs, OCFAs, and BCFAs.

Session B3: Informatics & Lab Management
B12

Creating a Reference Interval Database to Support Clinical AI/ML Applications with Generalizable Laboratory Phenotypes

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Background: Laboratory measurements are one of the most objective data sets created during clinical care. With the rapid growth in artificial intelligence and machine learning (AI/ML), these data are a key analyte to develop AI/ML models that rely on real-world data. However, the use of raw laboratory values can lead to issues in generalizability as models move from development to multi-site implementation as the interpretation of individual values can vary based on the local reference interval for individual assays. Clinically, laboratory test results are implemented with a set of rules to inform clinicians which results are abnormal, but while these ranges can also be used in the development of local AI/ML models, scaling this data preprocessing across institutions is a challenge. Methods: We developed a data model that can be used to store institutional reference intervals in an openly available database to enable community-based research for AI/ML applications. As part of this work, we evaluated the frequency at which discrepancies are observed between institutional reference intervals. In addition, we explored the development of categorical laboratory phenotypes based on reference intervals to create a semi-automated computational approach to preprocessing laboratory data, as initially described by Robinson and colleagues (2019, PMID: 31119199). Results: We developed a component-based data model for representing the reference interval values with records mapped to LOINC and SNOMED codes. Additional metadata were included to allow for queries of reference intervals based on the standardized codes, patient sex and age. We modeled data from six hospitals at a single system along with an independent and geographically distinct children's hospital. Even within a single health system, marked variations in reference ranges for common test components, such as lactate dehydrogenase, are present. Inclusion of reference ranges with individual laboratory measurements can subsequently be used to translate results into laboratory phenotypes for downstream applications. Conclusion: Development of a data model to represent and share variations in reference intervals provides an important resource for future research and to identify areas of variation within and among laboratories. With the use of common ontologies, these data can also be used to create generalizable phenotypes for clinical AI/ML applications.

Session B3: Informatics & Lab Management
B13

Evaluating the Utility and Challenges Associated With "Anonymous" Patients in the Electronic Medical Record

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Electronic medical records (EMRs) allow for the creation of "test" patients that can be used for training new users, testing changes before they go "live", simulating the placement of orders, or for a range of similar applications. Test patients are commonly utilized in EMR validation, support, or "playground" environments that might use a copy of the production EMR database but do not connect to the official medical record to prevent billing errors or patient harm. However, there are a variety of cases where it is useful to have test or anonymous patients within the EMR production environment as well. One example of this is infectious disease testing for employee blood-borne pathogen exposure (e.g., needlestick injury) that may need to be stored in a de-identified or restricted manner to comply with workplace privacy regulations. There are also instances, generally in emergency situations, where a medical record is created for a patient about whom little identifying information is known. In this example, these so-called "anonymous" patients are assigned random or arbitrarily pre-determined birthdates (e.g., 1/1/1900) and on occasion have no sex assigned in their chart. This poses a variety of challenges from a laboratory standpoint as it can be difficult to provide accurate normal ranges for laboratory results that are age and/or gender specific. Additionally, this has on occasion resulted in an inability to identify appropriate blood products as these recommendations are similarly based on age and gender. Another layer of complexity comes as additional information regarding the patient is made available, and health care information services merges data from a previously anonymous account to a specific patient record. Such mergers can result in cancellation of pending orders, errors in reporting laboratory results, or other complications depending on the specific process utilized. Surprisingly, there is little to no literature regarding the use cases for these "test" and "anonymous" patients or the challenges associated with their existence in the EMR. To explore this topic, we identified three classes of patients in our institutional EMR: true virtual "test" patients, "anonymous" patients that were subsequently identified, and "anonymous" patients that were never identified. Basic characteristics of these patients (sex and date of birth) and available laboratory results were compiled. Along with this, we present a series of instructional cases adapted from actual patient safety events at our institution involving anonymous patient records. These illustrative cases highlight the utility of these "test" and "anonymous" patients, as well as the challenges these pose on an institutional and individual level. Lastly, we provide recommendations on how best to manage similar scenarios that may arise.

Session B3: Informatics & Lab Management
B14

Recycling Opportunities in a High Volume Academic Clinical Chemistry Laboratory

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Many sectors of industry, including the biomedical sector, have quantified waste, and created sustainability strategies to mitigate its environmental impact. One of these strategies utilizes the waste hierarchy, a model which ranks the concepts reduce, re-use and recycle in order of the most to least sustainable practice. However, to date, the clinical laboratory has seldom been evaluated for total waste production and mitigation strategies and additional public reporting of the physical amount of waste produced in these areas are lacking in the literature. In this study, we aimed to identify specific wastes produced from performing the CMP over the course of a year in our automated clinical chemistry laboratory and what proportion would be recyclable. The total in- and outpatient testing volumes as well as volumes of quality control and calibrations needed to perform the CMP at our institution were collected retrospectively from 07/14/2021 - 07/14/2022. We further identified disposables waste items such as calibrator kits, quality control kits, patient blood specimen tubes, shipping packaging and reagent wedge kits that are necessary to perform the CMP. In addition, to obtain a conservative and consistent evaluation to the total amount of waste produced from the CMP, the average weights for components of the reagent test wedge kits which includes plastic wedges, cardboard shipping boxes, and paper package inserts were calculated. These weights in conjunction with total testing volumes was used to determine the total, recyclable, and non-recyclable waste produced from these disposable items. A total of 1089.2 kg of reagent kit wastes were estimated to be produced by performing the CMP over the course of a year. Of this waste, cardboard shipping boxes and paper package inserts were determined to be recyclable (233.6 kg) and the plastic reagent wedges were determined to be non-recyclable (855.5 kg) as they were not labelled with the universally recognized recycling code, were composed of proprietary plastic material, and contained biohazardous contaminants. Overall, 21.4 % of the total specific waste weight was found to be recyclable. The CMP is a small subset of the clinical chemistry test menu that produces a considerable amount of recyclable and non-recyclable waste.

Session B3: Informatics & Lab Management
B15

Analysis of Daratumumab Reporting in Type and Screen Orders to Identify Opportunities for Information System Improvement

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The rapid growth of monoclonal antibody therapies has resulted in a wide variety of targeted treatments for malignancies. The presence of these antibodies in patient plasma can interfere with blood bank testing, which in turn can create a delay in the process of pretransfusion testing and provision of blood products to patients. Availability of information regarding particular medications can help guide blood bank processes and testing algorithms. Reporting of patient medications that can interfere with blood bank testing, including targeted therapeutic antibodies (e.g. anti-CD38 therapies such as daratumumab), often relies on the ordering provider to provide that information. At our institution, the type and screen (T&S) order contains a prompt that requests the history of daratumumab administration. Available responses are “yes”, “no”, or “unknown”, with the default answer of “unknown”. The goal of this study was to evaluate the reporting practice of daratumumab history in the T&S order and identify potential areas for process improvement. We retrospectively reviewed T&S orders for patients receiving daratumumab therapy during 2022 at a single institution. Of 370 patients who were receiving daratumumab therapy, 214 (57.8%) had T&S orders. Forty of the 214 patients (18.7%) with T&S orders had at least one order with a “yes” answer indicating daratumumab administration. Of the 40 patients with an answer of “yes”, 16 (40%) were associated with the initial T&S after starting therapy. Of the other answer options, 23 of 40 (57.5%) indicated “unknown” and 1 (2.5%) indicated “no”. The remaining T&S orders ordered after the initial order were evaluated for consistency in response. Of 352 total T&S orders placed after the initial T&S orders, 62 (17.6%) were “yes” answers, 4 (1.1%) were “no” answers, and 286 (81.3%) were “unknown”. These results suggest that manual reporting of daratumumab therapy is not optimized at time of initial T&S orders placed after daratumumab treatment is started and is further misaligned with treatment status with subsequent T&S orders. Development of automated methods may help improve the process of reporting medications to the blood bank to guide testing. Future directions include development of an informatics-based approach to link the patient’s medical administration record (MAR) to the laboratory information system (LIS) to provide history of daratumumab therapy to the blood bank. This approach will prioritize: (1) compatibility with the blood bank’s current workflow for testing, (2) clinical needs for ordering laboratory testing, and (3) adaptability for reporting of other relevant interfering therapies to the blood bank as well as to other clinical laboratories.

Session B3: Informatics & Lab Management
B16

PathBrowser: An Educational Tool to Convert Textbook Images and Captions into Flashcards

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Background: Competence in reaching the correct diagnosis from analysis of clinical pathology specimens requires exposure to a large volume and breadth of cases. Images from textbooks are critical resources that supplement actual cases with well curated information. However, learning from textbooks has several setbacks. Images from individual textbooks are limited in number and often do not adequately capture variation of the disease entity. Textbooks also do not usually provide a platform for learners to assess their diagnostic abilities. This burdens the learner with creating flashcards for self-assessment, which is manually intensive. **Methods:** To address these limitations, we developed PathBrowser**,** a web browser-accessible program that leverages the PyMuPDF Python package (Artifex) to extract images and captions from textbooks in PDF format. Captions are written to the image files using ExifTool (Phil Harvey), making the images searchable by keywords. The program then displays the image while hiding the caption, challenging the user to enter the appropriate diagnosis. To minimize work by the user to prepare flashcard questions and answers, the program can automatically generate quiz questions by using natural language processing tools and a Naïve Bayes (NB) classifier (NLTK and SpaCy packages) to identify important terms from the caption as either diagnoses or cytologic features. **Results:** As a proof of principle, we used PathBrowser to build an image repository of myeloblasts and common mimickers, including reactive lymphocytes and chronic lymphoid leukemias, towards training junior pathology residents to identify blasts in peripheral blood and body fluids. In total, PathBrowser extracted 173 images (63 myeloblasts and 110 non-blasts) from 2 textbook sources (*Atlas of Diagnostic Hematology* by Salama et al., and *Hematopathology* by Jaffe et al.). We trained a NB classifier to label images as “myeloblast” or “non-myeloblast,” based on keywords in the caption. We manually ascertained that PathBrowser extracted the appropriate caption from 30/30 (100%) images of myeloblasts. Of these, the NB classifier correctly extracted the term “myeloblast” in 28 (93%) images. A survey of pathology residents showed that 89% of respondents agreed the program is a useful pathology learning tool. **Conclusions:** We developed a program that makes reading from textbooks an interactive learning experience. By automating the manual-intensive steps of extracting images and captions and preparing flashcards with quiz questions using caption terms classified by machine learning tools, learners can focus on recognizing the diagnostic features represented by the images. Finally, our program enables the rapid generation of a repository of images from diverse sources, so that learners can browse a wide spectrum of disease entities and their variants.

Session B4: Transfusion Medicine
B17

Trends In Hematopoietic Stem Cell Utilization and Cost of Cryopreservation

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Autologous stem cell transplantation (ASCT) is the standard of care treatment for multiple myeloma. Standard ASCT procedures collect hematopoietic stem cells (HPSC) in excess for multiple transplants due to reports of high mobilization failure and unsuccessful ASCT collections following myeloablative treatments. Cost analysis studies estimate that one year of cryopreservation and one day of HPSC collection would each cost $5000 per patient. Limited data is available on the usage of the second transplant and the storage costs of non-transplanted products. This study evaluates the utilization of cryopreserved HPSC products and calculates the cost of cryopreservation. A retrospective chart review study of a cohort of 240 deceased MM patients, who received ASCT between January 2010 to December 2015. Demographic and clinical data were obtained from the laboratory and electronic medical record. The cohort was categorized into two groups, with 130 patients in Group 1 (≤60 years) and 110 patients in Group 2 (>60 years). Cumulative incidence of a second transplant was computed from the life table using the Kaplan Meier method. The cost of cryopreservation was calculated based on the time HPSC products remained in the freezers before disposal. PBSC was mobilized using Granulocyte Colony Stimulating Factor (GCSF), or GCSF and Mozobil. The average age of patients at first collection is 61 (IQR: 54-66) years and the average age of death is 64 (IQR: 58 -70) years. The average life span of patients after receiving the first transplant is 3 (IQR: 2-5) years. The average number of collection days is 2 (IQR: 1-3). 65 patients had 1-day collections, 105 had 2-day collections and 70 had ≥3-day collections. 175 patients (73%) had >1 day collection. Only 22 patients (9%) received a second transplant and 18 of them (82%) were in Group 1 (≤60). The cumulative incidence of a second transplant by 5 years is 23% for Group 1 and 4% for Group 2. Two-transplant collections required 492 days of apheresis with an overall cost of $2,500,000; however, one-transplant collections would cost $1,400,000 for 279 apheresis days. The median cost of cryopreservation for each patient who did not receive the second transplant is $15,000 (IQR: $8000 - $25,000). Therefore, the estimated cost for all patients in the study is $3,600,000 until the disposal of HPSC products. The incidence of a second transplant is low across all patients and significantly lower in patients greater than 60 years of age. Cryopreserved stem cell products remain under-utilized, leading to substantial financial burden. The duration of HPSC collection and cryopreservation must be re-evaluated for future treatment plans. Institutional policies should be revised based on the utilization trend to lower the operational cost of storage.

Session B4: Transfusion Medicine
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A Stochastic Multicompartment Model of Hemostasis and Oxygenation During Trauma Resuscitation as a Platform for In Silico Trials of Transfusion

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Uncontrolled hemorrhage accounts for up to 40% of trauma related mortality, and approximately 30% of trauma related deaths occur in the hospital within the first 1-4 hours of injury. The Advanced Trauma Life Support (ATLS) guidelines still recommend initial resuscitation with crystalloid fluid as an integral part of maintaining or restoring hemodynamic stability, but are starting to recognize the role of early resuscitation with blood products in patients with evidence of Class III and IV hemorrhage, in line with recent clinical trial and observational data. Although there is a growing body of evidence that early transfusion with blood products may be associated with improved survival compared with crystalloid infusion, the optimal transfusion strategy still remains unclear and is being actively investigated in clinical trials. *In silico* models of resuscitation offer a means to evaluate the effectiveness and safety of resuscitation protocols, including effects on body fluid compartment volumes, tissue oxygenation, and hemostatic factors. Here we describe our work extending earlier deterministic models of trauma resuscitation to incorporate hemodynamic, hemostatic, resuscitation, biomarker, and tissue-oxygenation domains into a single comprehensive model. Additionally, this model expands upon previous deterministic models to create a stochastic computational model of hemostatic resuscitation that accounts for variations in blood component composition and temporal features of transfusion therapy. Using this stochastic model, an *in silico* trial was piloted to compare conventional component therapy, i.e. red cell, platelet and plasma components, to cold-stored whole blood using the following starting assumptions: patient weight of 81.3±21.8 kg, hematocrit of 41.8±4.3%, initial bleeding rate between 50 and 150 mL/min, systolic blood pressure of 125±18 mmHg, fibrinogen of 293±88 mg/dL, international normalized ratio of 1.0±0.1 and platelet count of 239±62x109/L, with blood component and whole blood constituent distributions based on laboratory quality control data. This *in silico* trial demonstrated that resuscitation with whole blood was associated with a 28-minute reduction in the time spent in the critical window defined by platelet count <50x10^9/L, INR≥2, hemoglobin <9 g/dL and fibrinogen <150 mg/dL compared with conventional component resuscitation over the course of a 4 hour simulation ($p<0.001$ based on median regression). We demonstrate how stochastic models of hemostatic resuscitation can be used to perform *in silico* trials of resuscitation strategies. Our work can guide inclusion and exclusion criteria for future clinical trials and facilitate identification of patient subgroups most likely to benefit from certain resuscitation strategies. This work was partially funded by the AABB Foundation (formerly the National Blood Foundation).

Session B4: Transfusion Medicine
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Residual Component Culture: Application of Standardized Transfusion Reaction Culture Criteria to Reduce Culture Rates

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Blood products are often cultured as part of a transfusion reaction (TRXN) workup in order to “not miss” a septic TRXN. These cultures are vulnerable to secondary contamination and are often challenging to interpret due to the lack of a corresponding patient blood culture. Although bacterial contamination of blood products remains a leading cause of transfusion related fatalities, the actual prevalence of primary contamination of blood components is quite low, leading to a low positive predictive value (PPV) for component culture. Given recently mandated mitigation strategies to reduce bacterial contamination of platelets, the PPV of component culture is likely to further decline, making appropriate selection criteria for culture even more critical to conserve laboratory resources and maximize clinical utility. At our institution the decision to culture is at the discretion of the pathology resident and/or transfusion medicine physician. We sought to review our current culture rates and determine if applying standardized indications for component culture could reduce culture rates without impacting diagnostic utility. Clinical symptoms and vital signs were reviewed for the 24-hour period after the reaction for all TRXNs reported from July 2021 to June 2022. Of the 105 reactions reported during the study timeframe, 39 (37%) were cultured, with one positive culture involving a platelet unit. This was deemed a true septic reaction given concordant cultures in the patient. Modified forms of the AABB and BEST culture criteria were then applied to the reported reactions. Modifications were made to provide specific definitions for tachycardia (heart rate > 100bpm and at least 15% increase) and hypotension (SBP < 80mmhg and at least a 30mmHg decrease). Application of the AABB criteria reduces the number of cultures to 22 (21% of reactions) whereas the BEST criteria increases the number of cultures to 51 (49% of reactions). Both criteria captured the true positive septic reaction. Neither criteria were completely concordant with our current practice. Of the 39 reactions selected for culture by our institution, 26 (67%) did not meet AABB criteria and 11 (28%) did not met BEST criteria; 9 and 22 different reactions would have been cultured based on AABB and BEST criteria respectively. Although we are not able to confirm if culturing of the discrepant units would have yielded additional positive cultures, retrospective chart review did not reveal any additional cases of clinically significant sepsis. The modified AABB criteria decreased the culture rate by 56% while still capturing the true positive septic TRXN suggesting that it would be the best option to reduce the cost/burden of culturing products without reducing diagnostic accuracy. Both published criteria do not take into consideration duration of symptoms and clinical interventions, thus clinical judgement remains critical to the decision to culture.

Session B4: Transfusion Medicine
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Did Interventions in a Massive Transfusion Protocol Program Change Transfusion Practice?

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Current literature supports improved clinical outcomes in the setting of trauma when a Massive Transfusion Protocol (MTP) adheres to transfusion at, or close, to a 1:1 ratio (RBC:Plasma). At our institution, between 2008 and 2015, the number of MTP activations increased ten-fold, accompanied by increased wastage of blood products and stress on the transfusion service. In response, in 2016-2018, we undertook an extensive root-cause analysis, and deployed multiple interventions, including clinician education and multiple process changes to the MTP, which succeeded in reining in inappropriate activation of the MTP, as we have previously published.
Heretofore, we have not addressed whether these interventions also affected the ratio of blood products transfused during MTPs activated at our institution. Here, we test the hypothesis that the changes deployed in 2016-2018 were associated with improved adherence to the desired 1:1 ratio.
The study is a retrospective analysis of massive transfusion data collected from 2008 to 2022. We reviewed RBC and Plasma units transfused to all patients receiving blood products through the MTP during this period. All patients transfused seven or more RBC and/or Plasma units following MTP activation were included in the study (total n = 443). Activations were classified by year. For each patient, the (RBC:Plasma) ratio transfused was calculated and assessed for adherence to a 1:1 ratio, with a ratio of 2:1 or greater classified as “suboptimal”. Our institution does not use Whole Blood.
MTP usage at our institution gradually increased from 2008, when the MTP was established, to 2016, when the MTP procedure was revised. Suboptimal transfusion ratios (RBC:Plasma) also increased from 2008-2016. Between 2008 and 2013, 15% of patients received suboptimal ratios following MTP activation. In 2014-2016, suboptimal ratios were observed in 25% of MTPs. Following multiple interventions, the frequency of MTP activation dropped precipitously, as described, and was accompanied by a decrease in the percentage of suboptimal ratios; in 2020 to 2022, 11% of MTPs involving seven or more transfused units had a suboptimal ratio.
In summary, the dramatic increase in activations of the MTP observed between 2008 and 2016 at our medical center was accompanied by an increase in suboptimal RBC:Plasma transfusion ratios. Interventions deployed between 2016 and 2018 led not only to reduced blood wastage, and lower stress of BB staff, but also to improved adherence to best transfusion practices, in the form of appropriate (RBC:Plasma) ratios transfused during MTPs.

Session B4: Transfusion Medicine
B21

Developing a Flow Cytometry-based Approach to Measure Post-transfusion RBC Survival

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Red blood cell (RBC) transfusion is the most common therapeutic procedure in hospitalized patients. Although transfusion can improve tissue oxygenation and perfusion, RBC units vary in their functional capabilities. Much effort has focused on defining RBC quality parameters that predict post-transfusion recovery, which relies on tracking transfused biotin- or 51-chromium-labeled RBCs in healthy adult volunteers. These approaches have limitations, including the need for pre-transfusion processing and the difficulty in performing these studies in allogeneically-transfused patients. Our goal is to develop a flow cytometry-based assay to distinguish several distinct RBC populations *in vitro* to model clinical transfusion scenarios. Thus, classical agglutination-based RBC phenotyping was performed for 3 individuals: #1 (blood group A, N-, K+); #2 (A, N+, K-); #3 (O, N-, K-). For RBC antigen detection by flow cytometry, *Ulex europaeus* lectin (UEA) was fluorescently labeled with Alexa-Fluor 488, monoclonal anti-N was detected with phycoerythrin-labeled anti-mouse IgG1, and monoclonal anti-Kell was detected with allophycocyanin-labeled anti-mouse IgG2b. Dose titrations were performed on $5x10^5$ RBCs to determine optimal antibody concentrations. Intra- and inter-assay variability (5 independent experiments, 5-10 replicates/experiment) were determined with antigen-negative and antigen-positive RBCs for each ligand individually; the percentage of RBCs staining positive was determined and the mean, standard deviation (SD), and coefficient of variation (%CV) were calculated. Inter-assay results (shown as [mean±SD, %CV]) were: N+ (97.5±5.5%, 5.6%), K+ (93.3±8.6%, 9.2%), UEA+ (97.4±4.0%, 4.1%). Small numbers of antigen-negative RBCs stained positively for N (1.26±0.7%) and K (0.43±0.5%). Because UEA binds H antigen, which is variably found with all ABO types, UEA also bound RBCs of individuals #1 (16.9±7.9%) and #2 (2.2±1.3%). Good precision and reproducibility were demonstrated by intra-assay CVs (<2%). To determine the limit of detection, K+ RBCs were titrated into K- RBCs using 2-fold dilutions from 10% to 0.005%. When plotted, the %K+ RBCs added and the %K+ RBCs detected by flow cytometry were highly correlated: slope of 0.96 and R^2 of 0.99. Adjusting for background (mean + 2*SD), as few as 0.025% K+ RBCs could be detected by flow cytometry within the 95% confidence interval. Finally, to simulate whole blood obtained from a transfusion recipient, RBCs from these 3 individuals were mixed at varying ratios down to 98:1:1. Using UEA, anti-N, and anti-K together, each individual RBC population could be identified and resolved in the mixture. These data show feasibility of using a flow cytometry-based assay to identify RBC populations from multiple individuals in a “mock” transfusion scenario, reliably detecting low frequencies of “transfused” RBCs. Because this does not require *ex vivo* processing and is minimally invasive, it is adaptable to monitoring short- and long-term post-transfusion RBC recovery in transfused patients and provides a platform for isolating individual RBC populations for subsequent functional analyses (e.g., metabolomics).

Session B4: Transfusion Medicine
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Preoperative Determination of Red Blood Cell Transfusion for Orthotopic Liver Transplantation in the Age of Artificial Intelligence

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Orthotropic liver transplantation (OLT) is a major surgical procedure associated with significant blood loss. Unanticipated blood requirements during OLT can delay the procedure and compromise lifesaving intraoperative resuscitation, adding strains to the blood bank and blood suppliers' resources, especially when units are requested on short-notice or for patients with alloantibodies. Age, preoperative laboratory values, severity of underlying liver disease, and coagulopathy are factors that influence the number of units required. Currently, each transfusion medicine service issues a specific number of crossmatched red blood cell (RBC) units for OLT patients. At our institution, 10 crossmatched units are issued for each patient, which may be an overestimation or underestimation of the number of units required for certain patients.
Aim: To characterize OLT patients who require more than 10 RBC units intraoperatively, and compare them to those who require less, identify pre-operative clinical and laboratory factors that predict which patients will require more than 10 units. Finally develop an artificial intelligence platform (AI-OLTRBC-1) aiming at reducing inappropriate RBC transfusions.
Methods: We collected data from 485 patients that underwent OLT from January 1st, 2021 to December 31st 2022. Data collected included demographics, coagulopathies, anticoagulants, ABO/RH group, and laboratory testing collected within 24 hours of admission (complete blood count, prothrombin time (PT), partial thromboplastin time (PTT), INR, ALT, AST, total bilirubin, conjugated bilirubin, alkaline phosphatase (ALP), creatinine, Blood urea nitrogen (BUN), calcium and thromboelastogram (TEG). Data analysis was performed in R-studio (V.1.4.1). Missing values were imputated using multivariate imputation by chained equations algorithm. AI-OLTRBC-1 was built using machine intelligence learning optimizer platform.
Results: Based on univariate regression analysis (p-value<0.05, 95% confidence interval) the following laboratory factors were found predictive of OLT patients requiring more than 10 RBC units: low albumin (OR 1.47 [CI 1.05-2.04]), increased total bilirubin (OR 1.06 [CI 1.041.08]), increased conjugated bilirubin (OR 1.08 [CI 1.04-1.11], increased creatinine (OR 1.55 [CI 1.33-1.83]), BUN (OR 1.03 [CI 1.02-1.04]), low hemoglobin (OR 1.61 [CI 1.81-1.42]), MCV (OR 1.04 [CI 1.02-1.07]), high INR (OR 3.48 [CI 2.35-5.26]), PTT (OR 1.04 [CI 1.03-1.06]), TEG-coagulation index (OR 1.12 [CI 1.05-1.19]). Among the anticoagulants, patients on enoxaparin required more RBC units (OR 1.47 [CI 1.66-11.1]). Other factors including demographic and ABO/Rh were not significant. The median number of transfused RBC units in patients requiring more than 10 units was 20, while the median number of transfused RBC units in patients requiring less was 5.
Conclusions: Our study aimed to characterize OLT patients who required more than 10 units and identified preoperative factors to estimate RBC unit requirements, which would aid transfusion medicine service in providing RBC units properly and on-time. AI-OLTRBC-1 achieved a sensitivity of 88.0%, specificity of 70.4%, and an accuracy of 71.8% in classifying patients.

Session B5: Molecular
B23

Simplifying Molecular Testing Through Electronic Order Entry

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Our solid-tumor molecular laboratory receives more than 3,000 orders each year, with about two-thirds coming from internal providers. Before this project, molecular tests were ordered using one of two different paper forms, which the care team then faxed or e-mailed to the Genetics Preanalytical Service (GPS). These requests led to frequent modifications and cancellations due to the complexity of molecular testing. A small fraction of requisitions were lost due to transmission errors. We undertook a project to design, develop, and implement computerized physician order entry (CPOE) in Epic (Epic Systems Corp., Verona, WI) and Sunquest (Clinisys, Tucson, AZ). We conducted extensive interviews with the directors of the molecular lab, laboratory medicine IT, GPS, anatomic pathology staff, laboratory scientists, laboratory genetic counselors, oncologists, clinicians, and nurse coordinators. The order itself and other technical changes underwent iterative review and testing by a subset of interviewees. Five oncologists participated in formal beta-testing.The user interviews allowed us to produce a detailed process diagram that drew attention to specific areas of repetition or risk. We proposed a new workflow that would eliminate repetition, provide redundant order-tracking, and automate some lab processes. Once approved, we built the electronic order in Epic and modified existing laboratory programs and interfaces as needed. The process of placing an order, which previously typically involved both nurses and doctors over several calendar days, was now being completed in fewer than 5 minutes by a single practitioner. Requisition status events were no longer created manually in Sunquest by GPS. Certain data-entry tasks were eliminated through the incorporation of label printers. Within one month of launch, more than 50% of somatic molecular orders arrived via CPOE, increasing to 90% within six months. At a rate of 125 CPOE orders per month, time savings range from 20 hours per month for GPS staff, 50 hours per month for nursing, and 20 hours per month for physicians. The success of this project demonstrates the feasibility of replacing a paper-based process for a complex test menu with CPOE. Due to the intricacies of molecular testing, such a change will undoubtedly involve multiple divisions. We attribute the success of this project to early involvement by key stakeholder groups, including developers; an extended testing phase to ensure reliability at roll-out; creation of straightforward reference documents; and rapid response to user questions, especially during the first weeks post-launch.

Session B5: Molecular
B24

Strategies For Validation of a Low-volume BCR::ABL p190 Assay in the Clinical Laboratory

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Background: The low prevalence of samples positive for the *BCR::ABL* p190 (e1a2) fusion transcript (<1/week) can be a barrier for molecular test validation. The Cepheid Xpert BCR-ABL Ultra p190 Assay is a single-use cartridge-based RUO assay designed for the quantitative detection of *BCR::ABL* p190 from fresh specimens. The following study describes our validation strategy to overcome this barrier for implementing a quantitative molecular LDT.
Methods: This study was conducted in a hospital clinical laboratory setting between 2019 to 2023. RNA was extracted and frozen from peripheral blood (PB) and bone marrow (BM) samples that were sent in parallel to a reference lab for *BCR::ABL* p190 testing. High positive diagnostic specimens (>10% p190/ABL1) were presumptively identified as *BCR::ABL* FISH positive and p210 negative. Diagnostic specimens were diluted in known negative PB or BM to achieve %p190/ABL1 in various quantitative ranges. Reverse transcription, amplification, and quantitative real-time PCR were performed in a single reaction format (Cepheid Xpert cartridge®). For accuracy determinations, reported results of clinical samples from the reference lab were compared to the obtained values from our validation using extracted RNA only. Banked proficiency testing (PT) material was used to supplement qualitative and quantitative accuracy. For precision, Invivoscribe (IVS) control material (San Diego, CA) diluted in seven levels (12.5% to 0.0031%; 4-fold increments) and Maine Molecular Quality Controls (MMQCI, Saco ME) at 10%, 1%, 0.1%, 0.02%, 0% were run by at least three technologists and rotated amongst the 16 instrument modules. To evaluate linearity, IVS controls at 15 levels (100% to 0.003%; 2-fold increments) were assayed in triplicate. Limit of detection (LoD) was the minimum concentration at which the detection rate is 100% in 10 independent runs. For analytical specificity, high-positive p210 specimens (>10%) were evaluated for detection of p190.
Results: a total of 169 samples were analyzed (33 BM, 32 PB, 5 PT samples, 73 IVS controls, and 26 MMQCI controls). We found a correlation (linearity) between reference lab results and clinical/ control samples (R-squared ~0.88, $P < 0.01$). Overall Cohen's kappa concordance for qualitative accuracy analysis was 0.80 (CI 95% 0.65-0.95). Sensitivity, specificity, and accuracy were 91%, 92%, and 91%, respectively. This assay showed precision in all levels of dilution (IVS and MMQCI samples) as previously established. LoD was 0.02%. Samples with high level of p210 /ABL remained negative with the p190 assay.
Conclusion: in the setting of low-volume assays optimized for fresh samples, such as for the detection of *BCR::ABL* p190, dilutions of clinical samples, banked frozen RNA extracts, PT samples, and commercial controls are important tools for validation of a quantitative LDT.

Session B5: Molecular
B25

Optimized Method to Enhance the Limit of Detection for Large FLT3 Internal Tandem Duplications

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Internal tandem duplications (ITDs) in the fms-related tyrosine kinase 3 gene (FLT3) are recurrently detected in acute myeloid leukemia (AML) and are associated with a poor prognosis. Evaluation for the presence of ITDs in AML is considered standard of care; detection alters risk stratification and therapeutic selection. ITDs can range in size, being a minimum of three base pairs to over 300 base pairs. Larger ITDs are considered rare; however, it is unclear whether this represents true prevalence or a consequence of conventional assay design. The FDA-approved companion diagnostic test for the detection of FLT3 ITDs has a six times higher limit of detection for large ITDs (~300 bp) compared to medium or small ITDs. Further, the conventionally used short-read sequencing approaches to detect ITDs can also struggle to detect larger duplications. Therefore, it is unknown how many patients may have large ITDs that have gone undetected. We developed an approach to improve the detection limit for large ITDs that uses polymerase chain reaction (PCR) and capillary electrophoresis (CE) with a spiked-in reference. Larger ITDs undergo a predictable and reproducible negative PCR bias, which can be adjusted once the effect has been quantitatively characterized. FLT3 ITDs are reported as an allele ratio, the ratio of the ITD to the wild-type allele, as a biomarker for prognosis; the spike-in reference allows for quantification of an allele ratio despite distinct CE run conditions for the ITD and wild-type alleles. Using existing commercially available controls and manufactured plasmid controls, sensitivity was optimized, including temperature, injection time, polymerase, and PCR primers. With this method, the detection limit for large ITD variants is comparable to the limit of detection for medium and small ITDs in the FDA-approved companion diagnostic assay. We now have a robust tool to evaluate the accuracy, precision, linearity, and limit of detection at different ITD lengths. Enhanced identification of large FLT3 ITDs may modify the prevalence estimates of large ITDs in AML and ultimately alter patient management.

Session B5: Molecular
B27

Tissue Fixation Significantly Impacts MLH1 Promoter Methylation Analysis: A Quality Improvement Study

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MLH1 promoter methylation (MPM) analysis is an invaluable tool for distinguishing sporadic from inherited colorectal and endometrial cancers. At our institutional clinical genomics lab, we observed an unusually high failure rate of MPM testing in endometrial (EM) cancers. This triggered a quality improvement (QI) project to identify the underlying cause and improve the success rate of our MPM assay. We retrospectively identified all MPM cases (EM and non-endometrial (NEM) cancers) between January 2019 and October 2022 through querying our departmental database. The failure rates of these two groups were juxtaposed with the following variables: DNA concentration, performing technologists, operating surgeons, and specimen collection day (Monday through Saturday). A subsequent fishbone analysis was performed to evaluate the impact of specimen handling, fixation, and embedding procedure/timeline in the gross room and histology labs. We identified one-hundred thirty-one EM cases and eighty-two NEM cases that underwent MPM testing. Thirty-one EM cases (24%) and seven NEM cases (9%) failed, re-demonstrating the higher failure rate (X2=7.9, P-value=0.005) of EM cases. There was no significant difference in DNA concentration, performing technologists, and operating surgeons when compared to passed cases, however, a highly significant difference was seen concerning day of specimen collection (X2=53, P-value<0.0001). Most notably, all failed EM (n=31) and NEM cases (n=7) were collected on either Thursday or Friday (failure rate of 26% and 59%, respectively, 44% jointly). Our fishbone analysis revealed that specimens accessioned Thursday afternoon and Friday were fixed throughout the weekend before embedding on Monday, resulting in prolonged fixation (one extra day). This is consistent with previous studies' conclusions showing DNA quality (but not quantity) significantly worsened with longer formalin fixation. Upon presenting these data to lab personnel, workflow changes were implemented. Cancer tissue that would have originally fixed over the weekend was instead processed on Saturday starting December 2022. This QI project revealed that prolonged formalin fixation of specimens over the weekend dramatically reduces the success rate of MPM analysis of EM cancer cases. Subsequently, we expanded our investigation to include other molecular assays at our institution that have returned similar results. Since the implementation of the revised workflow in December 2022, a preliminary prospective analysis showed the MLH1 failure rate of EM cancer tissues collected on Thursday and Friday has decreased from 44% to 11% in the past three months (December 2022 – February 2023). The current findings have important implications for the use of FFPE specimens in genetic analysis and highlight the need for careful consideration of fixation workflows, especially over the weekend, in sample processing protocols.

P01

Retrospective Evaluation of Mycoplasma Genitalium Prevalence and Macrolide Resistance in a Study Cohort of Pregnant Women in Central Alabama from 1997-2001

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Background: *Mycoplasma genitalium* (MG) is a highly prevalent STI and limited data suggest it could be associated with adverse pregnancy outcomes. Macrolides are the only MG treatment available in the U.S. that are considered safe in pregnancy. We recently published findings of an MG prevalence of 8% and a frequency of macrolide resistance-associated gene mutations (MRMs) of 41% in 224 pregnant women in central Alabama who were prospectively enrolled from 2020-2021. **Methods:** In the current study, we obtained stored cervicovaginal specimens and limited sociodemographic data from an earlier cohort of pregnant women in central Alabama, enrolled from 1997-2001 in studies evaluating preterm birth risk so that we could investigate changes in the prevalence of MG and MRMs in the population in the same city between the two time periods. Nucleic acid amplification testing for MG, as well as for *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis* was performed using the Cobas assays (Roche Diagnostics). MG-positive specimens were tested for MRMs in domain V of the 23S rRNA gene by real-time PCR. **Results:** Of 203 women with specimens available for testing, MG was detected in 23 (11.3%) and frequency of co-infection with other STIs was: *T. vaginalis* 11 (47.8%), *C. trachomatis* 8 (34.8%), and *N. gonorrhoeae* 2 (8.7%). Of the 23 MG positive specimens, MRM genotyping was successfully performed on 11 and there were no MRMs detected in these specimens. **Conclusions:** We found the prevalence of MG and co-infections was high in this remote study cohort of pregnant women, yet MG MRMs were absent, which supports the notion that macrolide resistance in MG has evolved within the last 20 years in this population of pregnant women and is likely related to macrolide use in the population. Strategies to limit macrolide use are needed to limit further resistance development that will make MG treatment challenging in pregnant women.

P02

Prevalence of Bacteremia Due to Streptococcus/Enterococcus Species at an Academic/Community Health System Over a Five-Year Period

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Timely surveillance of bacteremia is important for identifying emerging pathogens and to implement effective antimicrobial strategies and public health measures. Organisms in the genera *Streptococcus* and *Enterococcus* are often the cause of bacteremia and merit particular attention. The objective of this study was to determine the prevalence of bacteremia caused by several clinically significant *Streptococcus* species (*S. pyogenes*, *S. agalactiae*, *S. pneumoniae*, *S. dysgalactiae/equisimilis*, the *S. anginosus* group (*S. anginosus*, *S. constellatus*, *S. intermedius*), and *Enterococcus* species (*E. faecium* and *E. faecalis*) over a 5 year period (2017-2022). Bacteria isolated from blood culture bottles were identified by MALDI-TOF mass spectrometry (VITEK® MS). Data were obtained from a Laboratory Results Repository in Epic Beaker to include these organisms, isolated in blood cultures (BCs), patient gender, patient age, and the collection date. The data were then consolidated to yield one unique organism per patient per episode. The prevalence of organisms as a percent of the total positive BCs for the overall time period and for each year was determined. Species from the *Enterococcus* genus were the two most prevalent organisms for each year except for 2017. *E. faecalis* was the most prevalent overall (57.4%, n = 534) and for each year except for 2020. Combining all analyzed organisms**,** *S. agalactiae* was the third most prevalent organism for each year except for 2017 when it was the second and 2020-2021 when it was the fourth. However, within the *Streptococcus* genus alone, *S. agalactiae* was the most prevalent (27.5%, n = 281). *S. pneumoniae*, demonstrating seasonality, was the second most prevalent from 2018-2019, however, it was outranked by *S. dysgalactiae/equisimilis* from 2020-2022 when it was the fourth and by the *S. anginosus* group in 2017 and 2020-2022. *S. pyogenes* was the fourth most prevalent organism in 2017 and the third most in 2018; however, it decreased in subsequent years and was surpassed by all other organisms. Stratified by decade of life, patients in their seventh decade of life (60-69 yr) accounted for the most positive BCs for every organism, except for *E. faecalis,* followed frequently by patients in their sixth (50-59 yr) and eighth (70-79 yr) decades of life**.** Patients in their first decade of life (0-9 yr) accounted for a preponderance of positive BCs for *E. faecalis*, *S. agalactiae* (highest prevalence <7 days of life), and *S. pneumoniae*. This study highlighted the relative abundance of bacteremia caused by *Enterococcus* species. Additionally, it demonstrated the importance of *Streptococcus agalactiae* bacteremia, especially in the first and seventh decades of life. Finally, this study showed the increasing prevalence of organisms within the *Streptococcus anginosus* group and *Streptococcus dysgalactiae/equisimilis*. This analysis demonstrated the dynamics of bacteremia and prevalence among several species within the *Enteroccocus* and *Streptococcus* genera.

P03

In Vitro Analysis of Potential Drug Loss of Tacrolimus and Modified Cyclosporine Via Nasogastric Tube

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*Introduction***:** There is a lack of data regarding administration of immunosuppressive agents such as tacrolimus or modified cyclosporine via nasogastric (NG) tube. The current guidelines recommend avoiding NG administration of these drugs; however that is not always feasible, especially in the pediatric population. *Objectives*: The purpose of this study is to perform an in vitro analysis to measure drug concentrations before and after simulated administration of tacrolimus or modified cyclosporine via NG tube to determine how much drug loss occurs. *Methods*: Extemporaneously prepared tacrolimus suspension and commercially available modified cyclosporine solution were measured before and after passing through polyurethane NG tube of different sizes that are commonly used in the pediatric population. Each collected sample was considered one pass and repeated two more times using the same tube. A set of 3 passes was repeated 6 times for each size of tubes. *Results:* There is no significant decreases after passing through the polyurethane NG tube for both tacrolimus and modified cyclosporine. The percent change between actual and expected concentration of tacrolimus shows an average difference of 2.1% for the 6Fr 56cm tube, 1.2% for the 6Fr 91cm tube, and 1.0% for the 8Fr 91cm tube. The modified cyclosporine shows an average difference of 13% for the 6Fr 56cm tube, 18% for the 6Fr 91cm tube, and 17% for the 8Fr 91cm tube. The higher-than-expected concentrations after passing through the NG tubes are likely due to measurement errors. *Conclusion*: The results support the use of NG administration of extemporaneously prepared tacrolimus suspension and commercially available modified cyclosporine solution, as no loss of drug dose was observed after passing through the NG tubes.

P04

Comparing Refrigeration to Immediate Room Temperature Testing for Uric Acid Monitoring in Rasburicase-Treated Patients

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Rasburicase (Rb) is a uric acid (UA) degrading enzyme important for treating tumor lysis syndrome. Rb retains activity at room temperature (RT), so specimens collected for UA-level monitoring require cooling protocols: collecting samples in pre-chilled tubes, transporting on ice, centrifuging at 4°C, and testing within 4 hours. In our laboratory, specimens are tested within ~45 minutes of collection. Our clinical study objective was to determine if we could ease these pre-analytical requirements to improve compliance while maintaining accuracy. 50 pairs of specimens were transported and stored either on ice or at RT. All were tested at 3 time points post-collection: immediately upon arrival to the laboratory (~45 minutes), 90 minutes, and 135 minutes. Linear regression analysis of iced versus RT specimens showed a high correlation with R^2= 0.99 (p< .0001) and bias of -2.4%, which indicate no clinical differences observed in UA concentrations between 1-12 mg/dL, at the immediate testing time point. UA levels did not significantly decrease in the iced specimens at any time point. However, UA levels had decreased by >10% in 16 of the 50 RT specimens after 90 minutes. Linear regression analysis of specimens tested immediately on ice versus RT specimens tested after 135 minutes yielded an R^2= 0.84 (p< .0001) and bias of -17.5%. The best model from a stepwise regression was composed of the number of binned Rb half-lives (0-2 or >2) that had passed since the patients' Rb infusion (Rb half-life= 1080 minutes; p< .0001) and the Rb dose (3 mg versus 6 mg, p< .0001), which explained ~50% of the UA variation (R^2= 0.48, p< .0001). Keeping Rb dose constant, RT specimens tested within 0-2 half-lives post-infusion had an additional 24% average decrease in UA concentration compared to those tested after >2 half-lives. Similarly, keeping Rb half-life constant, RT specimens from patients given a 6-mg dose had an 18% decrease in UA concentration compared to patients given a 3-mg dose. Using a total allowable error (TEA) of 17% as a threshold, 96%, 60%, and 38% of RT specimens tested within 0-2 half-lives were within TEA at the immediate (45-minute), 90-minute, and 135-minute time points, respectively. In contrast, 100%, 96%, and 88% of RT specimens tested after >2 half-lives were within TEA at the immediate (45-minute), 90-minute, and 135-minute time points, respectively. UA concentrations are not clinically different in RT or iced specimens, as long as tested within ~45 minutes post-collection. Specimens tested within 2 Rb half-lives post-infusion have significantly decreased UA levels if kept at RT for >90 minutes. Laboratories that can test UA levels rapidly after specimen collection may be able to validate alternative pre-analytical methods to transporting and testing on ice.

P05

Point-of-care HIV Testing Send Outs Integration in Laboratory LIS Using the NOVA StatStrip Glucometer

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Post-exposure prophylaxis is considered a highly effective preventive measure in reducing the cases of HIV transmission post occupational blood exposure if started within 72 hours. Point-of-care testing (POCT) for HIV antigen/antibody has aided in the rapid determination of HIV infection and initiating treatment. However, a molecular test is needed to confirm positive results of an HIV POCT, which involves a manual send out request. A 2021 survey identified 4.5% of reactive screening test results that were missed or sent to the wrong laboratory due to manual entry errors. We investigated the use of the NOVA StatStrip glucometer to record the results of the HIV ½ antigen/antibody test results into the laboratory information system through QML Telcor middleware software. A new test entry was developed on the NOVA StatStrip and an automatic reflex rule was developed to allow send out testing to be generated by the laboratory system and circumvent issues with manual entry. A POCT confirmatory rule was successfully developed to create send outs that reflexed for confirmatory testing. The reflex rule was tested and validated using the Abbott HIV ½ antigen/antibody test recorded on the glucometer. A reactive result for HIV ½ antibodies would add an HIV ½ antigen/antibodies testing order. A reactive result for the HIV ½ p24 antigen creates a send out request for HIV-1 RNA molecular testing. If POCT HIV ½ test is reactive for both antibodies and p24 antigen, both HIV ½ antigen/antibody and HIV-1 RNA molecular testing is ordered through the QML Telcor middleware. The reflex rule was further validated and tested. No confirmation HIV molecular test orders were missed, and no incorrect orders were observed using the electronic data entry and automatic reflex for send outs. POCT using the HIV ½ antigen/antibody immunoassay allows for bedside or clinic screening for fast treatment response as well as post-exposure prophylaxis for healthcare workers. Our core laboratory demonstrated the effective use of glucometers to transmit results through QML Telcor to post on the laboratory information system and create an automatic confirmatory send out order based on reactive results. Thus, reducing errors associated with maunal send out orders.

P06

Performance of a Modified ALLType NGS HLA Typing Assay with the Ion Chef/Ion S5/TypeStream Visual System

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OBJECTIVES: The commercial ALLType assay (One Lambda, West Hills, CA) enables accurate, high-resolution typing of 11 HLA genes using the Ion Chef/Ion S5/TypeStream Visual (TSV) system. The assay features a multiplexed PCR to enrich all target HLA genes in a sample, and up to 48 samples can be indexed and sequenced in a run. The assay is laborious due to the late pooling of indexed libraries. Early pooling significantly simplifies the workflow but may increase the background noise and typing errors. This project aims to examine the feasibility of early pooling immediately after the indexing step and evaluate the performance of such a modified ALLType protocol. **M**ETHODS: A total of 75 unique samples with diverse HLA genotypes were included in this study, which comprised 52 proficiency testing samples of three different sources, 10 stem cell recipients, 7 stem cell donors (including 2 buccal swabs), and 6 deceased organ donors. Genomic DNA extracted from these samples was tested in four sequencing runs, with 15-31 samples per run, using the modified ALLType procedure (reagent lot: 15). The results were compared with the reference typings generated by the manufacturer-established protocol. All data were analyzed using TSV (version 3.0) and the IPD-IMGT/HLA library (version 3.47); the default analysis parameters were applied. The primary endpoint of the study was the concordance of 3-field typing results. The secondary endpoint was key health metrics, including allele balance, key-exon coverage, and background noise. We also evaluated the saving on hands-on time and reagents with the modified protocol. **R**ESULTS: The concordance rates of 3-field typing results were 100% for *HLA-A, HLA-B, HLA-C, HLA*-DPA1, HLA-DPB1, HLA-DQA1, HLA-DQB1, and *HLA-DRB*1, and 96.2% for *HLA-DRB3*/4/5. The three discrepant *HLA*-DRB3/4/5 results with the modified protocol were false positive allele calls due to a small number of contaminating reads, which were corrected by increasing the threshold for *HLA-DRB3/4/5* in TSV. The allele balance and exon 2 coverage across all samples and genes were comparable between the modified and reference protocols, with R-squared values of 0.83 and 0.81, respectively. High background signals in exons were observed in only 0.6% of all samples with both protocols. The modified protocol reduced the hands-on time by 15%, from 6.5 to 5.5 hours, and reduced the use of library preparation reagents by 30%. **C**ONCLUSION: It is feasible to pool indexed libraries early during the library preparation process without increasing the background noise in the sequencing data. The modified ALLType protocol showed typing accuracy and health metrics comparable to the original protocol, with significant savings on time and reagents.

P07

Utility of Blood Culture Bacterial Phenotype Confirmation of Rapid Molecular Identification: A Case Report

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While molecular diagnostics have decreased turnaround time in identification of bacterial pathogens causing human disease, these tools are not infallible. To illustrate this point, we present a case of mistaken identity in a patient with bacteremia. A 38 year old El Salvadorian male with no significant past medical history was admitted to the hospital for cerebral toxoplasmosis in the setting of newly diagnosed HIV/AIDS. On hospital day 10, the patient developed new onset diarrhea. Infectious work-up identified Giardia in the patient's stool by both antigen testing and microscopic examination for ova and parasites. Concomitant blood cultures grew Gram-negative rods, which were identified as CTX-M positive *Escherichia coli* by the BioFire® Blood Culture Identification 2 (BCID2) panel. In culture, an indole-negative, non-lactose fermenting organism was recovered from MacConkey agar. Matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) mass spectrometry (MS, Vitek MS) identified the pathogen as *E. coli*, but *Shigella* species could not be excluded. Laboratory protocol called for further testing, and subsequent biochemical testing (BioMerieux Vitek 2 System GN ID) identified the pathogen as *Shigella sonnei*. The identification of *S. sonnei* was confirmed by 1) in-house antigen testing using the Wellcolex™ Color Shigella assay kit and 2) testing at the state's Department of Public Health laboratory. Stool PCR analysis for enteric pathogens (Verigene EP) was performed on the previously submitted specimen. Testing was positive for *Shigella*, and *S. sonnei* was recovered from the stool specimen, suggesting a gastrointestinal source for the patient's bacteremia. While *Shigella* bacteremia is rare compared to E. coli bacteremia, it is more prevalent in immunocompromised patients, such as this patient. While *Shigella* cross reactivity with *E. coli* is identified in the BCID2 package insert, this case demonstrates the need for laboratories to correlate bacterial growth phenotypes and the patient's overall clinical picture when interpreting molecular testing methods.

P08

Caffeine, Lorazepam, and Morphine Use in Neonatal Intensive Care Unit Population and Potential Relevance of Pharmacogenomics

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Medications are critical for managing acutely ill infants in neonatal intensive care unit (NICU). Tailoring therapies to individual differences in response and dose requirements might help improve outcomes. However, tools for optimizing pharmacotherapy remain limited. In this retrospective study, we explored the potential utility of pharmacogenetics for commonly prescribed NICU medications. All patients admitted to our local NICU March-December, 2022 were eligible for inclusion in the study. In infants who received at least three doses of one or more medications, we extracted DNA from residual EDTA blood collected for routine clinical care according to IRB-approved study protocols. Demographic, pharmacy, and clinical information was recorded retrospectively. Targeted pharmacogenetics testing was performed with a custom TaqMan OpenArray and a QuantStudio 12K Flex (ThermoFisher Scientific) with DNA normalized to 50 ng/mL. Results were analyzed using Genotyper Software version 1.3 and allele calls were made based on the combination of variants detected and consensus nomenclature. For drugs administered to at least 30 NICU patients, pharmacogenes were evaluated for variant allele frequency and potential clinical relevance. Of the 132 patients enrolled, 81 were male. Average length of stay was 47 days. Of the 64 different medications prescribed to at least one infant, for 15 of them are described clinical annotations with specific pharmacogenes by the PharmGKB and/or Clinical Pharmacogenetics Implementation Consortium. Of those 15 medications, three were administered at least three times to at least 30 infants: caffeine (n=102), morphine (n=56), and lorazepam (n=31). The associated pharmacogenes were *CYP1A2* (caffeine); *CYP3A4, OPRM1, COMT, ABCB1* (morphine); and *UGT2B15* (lorazepam). Relevant to the rate of clearance of caffeine, rs2069514 *(CYP1A2)* was heterozygous in 18% of patients, and homozygous in 5%. Relevant to the rate of clearance of morphine, *CYP3A4*22* was heterozygous in 5%. The common variants associated with response to morphine, c.472G>A (*COMT*) and c.118A>G (*OPRM1*) were heterozygous in 43% and 26%, and were homozygous in 22% and 8%, respectively. The transporter variant *ABCB1*2* was heterozygous in 6% and homozygous in 11%. Relevant to the rate of clearance of lorazepam, *UGT2B15*2* (rs1902023) was heterozygous in 45%, and homozygous in 31%. Correlation of pharmacogenetic results to specific clinical phenotypes is currently in progress. Pharmacogenetic variants relevant to commonly prescribed medications in the NICU are prevalent. Further clinical correlation of pharmacogenetic results may help inform selection and dosing of medications for critically ill NICU infants. This research may also facilitate detection and definition of new drug-gene associations unique to this patient population.

P09

Evaluating the Performance of ChatGPT in Writing Autopsy Clinicopathological Correlations

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ChatGPT is a chatbot launched by OpenAI in November 2022 that has generated excitement due to its utility in several technical fields including medicine. The application has gained media attention due to concerns of academic plagiarism, including its use by students for writing projects. In scientific writing, a preprint in bioarxiv reports human reviewers failing to identify a portion of ChatGPT generated abstracts. Several articles published in early 2023 list ChatGPT as a coauthor, generating debate. In medicine, Gilson et al found ChatGPT crossed the 60% threshold for the NBME Free Step-1 dataset. Patel and Lam wrote a commentary examining the value of ChatGPT in writing discharge summaries. A literature review in PubMed yielded articles further examining the utility of ChatGPT in scientific writing, however none looking at its use in pathology report writing was found. To examine this, we investigated the capabilities of ChatGPT in writing autopsy clinicopathologic reports. The February 13 version of ChatGPT was used to generate autopsy clinicopathologic correlations using prompts with the same patient demographic, same medical history of hypertension and coronary disease, and varying autopsy findings. These findings include cardiac infarct, saddle emboli, basilar artery thrombus, liver cyst, and leukoplakia. A prompt with no significant autopsy findings was also included. The prompts note a lack of imaging, labs, and toxicology. The generated responses were examined and compared. ChatGPT generated multi-sentence responses incorporating patient information, history, and major autopsy findings per prompt, ranging in length from 8 to 14 sentences. Each output varied in style, with some responses including sections for gross and microscopic findings, while others only consisting of clinicopathologic correlation. Each response was generated between 42 seconds to 1 minute. The application generated plausible correlations between the medical histories and autopsy findings. ChatGPT correlated the findings to the patient's supplied history in prompts with a cardiovascular autopsy finding. For the liver cyst, ChatGPT linked cyst formation to portal hypertension. For leukoplakia, ChatGPT suggested the presence of an upper GI cancer with cardiovascular history also likely contributing to death. For the prompt without significant findings, ChatGPT noted that the autopsy was inconclusive. ChatGPT debuted with an increasing amount of media attention due to its capability of producing natural language responses and surprising knowledge within multiple technical fields. ChatGPT is currently being used in academic writing at multiple levels within multiple fields. In medicine, ChatGPT has done well in multiple USMLE question banks. This study found that ChatGPT generated coherent clinicopathologic correlations commensurate to the amount of information supplied in the initial prompt. While useful as an initial framework, human review is still necessary to refine the response to make a more coherent report and to review made-up findings and dubious correlations.

P10

Utility Of Vizient Clinical Data Base as a Benchmarking Tool for Laboratory Stewardship Programs

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Establishing an effective laboratory stewardship program across healthcare systems to improve patient care has been of growing interest. Despite general guidelines from various organizations, clear definitions for these laboratory-based quality measures, and associated benchmarks, are still lacking. Hence, we utilized Vizient® Clinical Data Base (CDB) as a tool to benchmark our institution against U.S. News and World Reports' Honor Roll (USNW) healthcare organizations 2021-2022. We focused on inpatient laboratory testing with specific targets including mean laboratory resource units used per patient per day to obtain an overview of our institution's overall performance, daily basic metabolic panel and CBC test ordering patterns across various service lines, and C-reactive protein (CRP) to erythrocyte sedimentation rate (ESR) order ratios compared to USNW hospitals. As one of the five institutions with the highest mean laboratory resource units used per case per day (12.7) from January 1, 2021-January 31, 2022, we investigated this further to identify tests driving this result. Of all the laboratory tests ordered, blood gas was identified at the 99th percentile compared to peers. Stratifying by service, we found cardiac surgery (17%), general medicine (15%), pulmonary/critical care (11%), neonatology (10%) and transplant (9%) services at our institution were the major contributors to blood gas orders. Investigating daily laboratory test orders (BMP, CBC) showed that our institution was at the 46th and 71st percentile overall, respectively. Further CBC analysis showed that general medicine (28%) and oncology (11%) services were the major contributors for the test volume and highest total resource units used per quarter in 2021. Assessing CRP to ESR ratio depicted that our institution's ratio of 2.2 was lower compared to USNW hospitals' average of 2.9, meaning ESR is likely overutilized. In conclusion, Vizient CDB can be used as a resource for benchmarking laboratory utilization patterns. It can be helpful in developing road maps and prioritizing interventions for lab stewardship programs. This study identified a general overuse of laboratory resources at the hospital compared to peers, and identified some intervention targets including blood gas testing and ESR.

P11

Characterization of PIK3CA Mutation Testing in Metastatic Breast Adenocarcinomas: A Multi-site, Single Institution Study

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Introduction: Detection of somatic mutations in advanced breast cancer may inform prognosis and therapy for patients. In ER+ breast cancer, nearly 40% of tumors have activating mutations in PI3 kinase (*PIK3CA)* for which targeted PI3 kinase inhibitors are available. At our institution, reflex ordered testing of *PIK3CA* in ER-positive, HER2-negative advanced breast cancers was implemented in 2017 to standardize the molecular biomarker testing in these tumors.
Methods: We analyzed 219 cases of advanced breast carcinoma diagnosed from 1/1/2017 to 12/31/2022 across the Houston Methodist system. With IRB approval, records were collated through full-text searching of interpretation, comment, and tumor synoptic fields in the anatomic pathology (AP) reports for "breast" and keywords for molecular oncologic testing, including "PIK3CA" and "MOLECULAR DIAGNOSTICS", and then manually reviewed to exclude indeterminate/undifferentiated carcinomas and carcinomas of non-breast sites. Only molecular tests performed within this timeframe were considered. *PIK3CA* testing, both single-gene and targeted panels, was performed in 179 cases. Turnaround time (TAT) statistics, defined as days from AP report signout to molecular signout, were available for 102 cases. Cases with TATs greater than 60 days and referral laboratory testing were excluded. Data extraction, transformation, and loading was performed in Microsoft SQL Server (SSMS 18.0) and VS Code (Python 3.6). Analysis was performed using R-4.2.1 and Microsoft Excel.
Results: *PIK3CA* mutation testing was performed in 179 of 219 (82%) cases of all specimen types. The most common reasons for lack of reflex ordered molecular testing included insufficient tissue quantity and specimen decalcification. At least one *PIK3CA* genomic alteration was detected in 57 of 179 (32%) of cases. The most common alterations included p.H1047R (23/179, 13%), p.E545K (18/179, 10%), and p.E542K (8/179, 4%). One case had *PIK3CA* amplification, and one case had co-mutations of *PIK3CA* (p.G106V, p.H1047R). 217/219 (99%) of patients were female; no *PIK3CA* alterations were identified in the 2 male patients. *PIK3CA* frequency was not associated with age (mean age 65.4 for *PIK3CA* alteration detected and 63.8 for not detected, p=0.41). Mean TAT was 16.4 days (n=102), and 56% (57/102) of cases were resulted within 2 weeks of AP reporting. 22% (40/179) of cases had *PIK3CA* performed at a referral laboratory, largely occurring during the COVID-19 pandemic.
Conclusion: A reflex ordered strategy for *PIK3CA* mutations in advanced breast cancers led to the prompt availability of appropriate molecular results for most patients. *PIK3CA* alterations were present in 32% of cases, with the most common mutations being p.H1047R, p.E545K, and p.E542K. No significant differences in *PIK3CA* alterations by patient age was observed. Some cases had extended TATs for molecular results, which may be due to ordering practices, the specific *PIK3CA* testing procedure, and test send-out. Further studies will investigate the association of *PIK3CA* mutations and clinical staging.

P12

Discordant Indirect Immunofluorescence Compared to Multiplex Bead Immunoassay in ANCA Associated Vasculitides, A Retrospective Analysis

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Based on the revised 2017 international consensus on testing for anti-neutrophil cytoplasmic antibodies (ANCA) in granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), we conducted a retrospective analysis to assess whether testing algorithm modification would be appropriate in our laboratory. Currently, at our institution, the primary screening method for ANCA associated vasculitides (AAV) remains indirect immunofluorescence (IIF), which is reflexed to immunoassay (IA) for confirmation. IA is performed by multiplex bead technology to detect anti-myeloperoxidase (MPO) and anti-proteinase 3 (PR3) antibodies. We reviewed cases from January 1, 2021, to November 30, 2022 using Softlab (laboratory information system) with the aim to find discordant results between IIF and IA (IIF-positive and IA-negative, and IA-positive and IIF-negative). We limited our analysis to in-house patients with clinical information available (EPIC electronic medical record). 204 cases met the criterion for positive IIF and negative IA (positive IA defined as index value >0.9), of which 5% were close to the cut off index value (0.7-0.9). 64% of these 204 patients were never concordant in results available for review (IIF-positive, IA-negative). Potential confounding factors for these never concordant cases include 44% historically or concurrently ANA-positive (10% with clinical diagnosis of lupus), 11% with inflammatory bowel disease, and 10% with an underlying ophthalmologic diagnosis, both overlapping with positive ANA. Notably 36% of the patients who were IIF negative over this period had historically positive MPO or PR3 testing, and the current testing window may reflect higher sensitivity of IIF methods, which in this population includes index values near cutoff but definitionally negative. In contrast, of 247 cases with IA-positive results, 51 cases were discordant with IIF results (IA-positive, IIF-negative). 57% of the discordant cases had a historical diagnosis of AAV who were receiving treatment or in remission. 34% of these AAV discordant cases were near the cut off index value (1.0-1.2). Furthermore, we found that all patients with a clinical diagnosis of AAV were monitored by serial laboratory testing at varying frequency, which included IIF with titers and IA (at least once). As there are no explicit guidelines for laboratory testing to monitor AAV patients, it is unclear whether ordering both assays is of clinical utility in management. With advantages of efficiency and faster turnaround time, IAs may be considered as the primary screening method. In our patient population, we did not identify patients who were IIF-positive only with clinically meaningful disease. Although there may be clinical scenarios that warrant to perform both assays simultaneously, for those with GPA and MPA we conclude that it may be appropriate to transition to use IAs as the primary screening method and use IIF as a confirmatory assay, which may not need to be repeated if positive once.

P13

Change in HbA1c Post-transfusion is Correlated to Pre-transfusion HbA1c Result

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Hemoglobin A1c (HbA1c) results are used to diagnose and monitor patients with diabetes mellitus. As such, they have a direct impact on patient care and treatment decisions. While within the laboratory community, there is the assumption that recent red blood cell (RBC) transfusion would interfere with HbA1c measurement, there is limited published evidence regarding whether HbA1c results provide an accurate estimate of long term glycemic control in patients who have received a RBC transfusion. This retrospective laboratory information system record review aims to address this gap in the literature with a retrospective analysis of patient results. Retrospective data was obtained from the laboratory information system. The study population included all patients over 18 years of age, both inpatients and outpatients, who had at least one HbA1c result during the study period (January 2018 – December 2020), and record of a RBC transfusion in the three months prior to the A1c result. Data collected included relevant laboratory results and transfusion information. 1,752 pre- and post-transfusion HbA1c pairs were analyzed. The average age of patients at transfusion was 66.0 years. Men comprised 51.7% of subjects (n=905). Most patients were White (64.0%; n=1,104), with Black (29.7%; n=513) and Multiracial / Multicultural (4.1%; n=71) subjects making up the largest minority. Most patients had diagnoses of anemia (93.0%; n=1,629) and/or diabetes (86.2%; n=1,511), with a minority having a diagnosis of any type of cancer (40.6%; n=712). Rarely, patients had hemoglobin disorders (3.1%; n=54). Most patients were treated with some form of glycemic control medication (91.5%; n=1,603). Average pre-transfusion HbA1c for all subjects was 7.0% ± 1.9 (1 sd). Average post-transfusion HbA1c for all subjects was 6.3% ± 1.3 (1 sd). The average change in HbA1c from pre- to post-transfusion was -0.7% ± 1.5 (1 sd). In contrast, the mean change in the random blood glucose measurement closest to the pre- or post-transfusion HbA1c was only -11.5 mg/dL (CI: -16.7 mg/dL to -6.2 mg/dL; $p<0.001$). The median time between the pre-transfusion HbA1c and transfusion was 20.0 days; the median time between transfusion and the post-transfusion HbA1c was 38.0 days. There was a larger decrease in pre- to post-transfusion HbA1c in patients with diabetes ($p<0.001$), patients without anemia ($p=0.040$), patients without hemoglobin disorders ($p=0.045$), patients without cancer ($p=0.005$), and patients on any glycemic control medication ($p<0.001$). Overall, pre-transfusion HbA1c level was strongly associated with post-transfusion HbA1c level, with the greatest degree of negative change seen in patients with a pre-transfusion value > 9.0%. In contrast, patients with a pre-transfusion value of < 5.7% saw an average increase in HbA1c ($p<0.001$). This study provides insight into the influence of transfusion on HbA1c results and reinforces the important role that pre-analytical factors play in laboratory testing.

P14

Evaluating the Effectiveness of Pseudothrombocytopenia (PTCP) Panel with Alternative Anticoagulants on Clinically Suspicious EDTA-Dependent PTCP: A Single Tertiary Hospital Experience

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EDTA is considered the most common anticoagulant to induce pseudothrombocytopenia (PTCP). PTCP panel with alternative anticoagulants (heparin and citrate) has been ordered by clinicians in our hospital for suspicious EDTA-dependent PTCP cases to obtain the correct platelet count (PC). In this study, we aimed to evaluate the effectiveness of alternative anticoagulants on clinically suspicious EDTA-PTCP. We retrospectively identified cases for which PTCP panel (EDTA, heparin, and citrate) was performed from June 2021 to March 2022 using the SAP business intelligence tool. PC was considered significantly different when the difference is more than 25% comparing heparin or citrate to EDTA tubes. Representative cases were chosen for chart review and/or peripheral blood smear review. 200 cases were included in the study. 76 cases had similar PCs in all 3 tubes which represent either true thrombocytopenia or PTCP in all 3 tubes. 17 cases had higher PC on heparin and/or citrate than EDTA which are EDTA-PTCP corrected by alternative anticoagulants (confirmed by smear review). Among those 17 cases: 6/17 had high PC on citrate only, 2/17 on heparin only and 9/17 had higher PC on citrate/heparin. 82 cases had lower PC on heparin only compared to EDTA and 62/82 had heparin exposure. There was 1 case with lower PC on citrate only (no heparin tube) compared to EDTA. 24 cases had lower PC in both heparin and citrate than EDTA tubes (lowest PC on Heparin) and 21/24 have heparin exposure. Peripheral blood smears were reviewed in 39 representative cases. Platelet clumps were identified in the corresponding tubes of all cases. Our study shows that heparin-PTCP is common in hospitalized patients and confirms that heparin is not a suitable alternative anticoagulant for EDTA-PTCP as shown by previous literature. However, many laboratories still use it for EDTA-PTCP. Heparin is known to promote platelet activation which may cause PTCP. The low PC in the heparin tube also seems to be associated with prior heparin exposure. Citrate is a better alternative to EDTA-PTCP. Among cases with low PCs on citrate, nearly all have low PCs on heparin as well. It is interesting to note those cases usually have lower PCs on heparin versus citrate and have prior exposure to heparin. The low PCs on citrate might be partially due to insufficient correction (110%) of PC by the dilution factor of the anticoagulant. Literature showed that a higher corrective factor of PCs is required for citrate. Therefore, a correlation study of PCs in EDTA versus citrate in each lab is needed to establish the corrective factor. Furthermore, delayed processing might be contributing as PCs on citrate are less stable and must be processed within 3 hours.

P15

Development and Validation of a Liquid Chromatography Mass Spectrometry Method to Measure Highly Concentrated Tacrolimus and Cyclosporine Specimens Prepared from Commercial Pharmaceutical Products to Assess Administration Through Feeding Tubes

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Background: Tacrolimus and cyclosporine are common immunosuppressive drugs used in the prevention and treatment of solid-organ transplant rejection (e.g., kidney, liver, heart). Other indications include several autoimmune diseases such as Crohn's disease, autoimmune hepatitis, and rheumatoid arthritis. To prevent toxicity while achieving therapeutic efficacy, tacrolimus and cyclosporine in whole blood specimens are commonly measured in medical centers so that their dosages can be precisely adjusted. Different from adult patients, pediatric patients often require smaller doses and the use of feeding tubes for drug administration. In order to assess nonspecific adsorption by feeding tubes, we modified our in-house clinical method to measure highly concentrated tacrolimus and cyclosporine specimens prepared from clinical pharmaceutical products.
Method: Highly concentrated tacrolimus and cyclosporine specimens were serially diluted with dimethyl sulfoxide (2,000 times for tacrolimus and 20,000 times for cyclosporine) before measurements by our clinical method using liquid chromatography mass spectrometry. The method for highly concentrated tacrolimus and cyclosporine was validated, with analytical measurement range determined with in-house prepared concentrated specimens at varying concentrations, precision (repeatability and reproducibility) assessed by multiple measurements of concentrated specimens at three different concentrations, accuracy assessed by recovery studies, and matrix effect assessed by post-column infusion and by matrix dilution with dimethyl sulfoxide.
Results: The method was linear from 10 ug/mL to 80 ug/mL for tacrolimus, and 1 mg/mL to 8 mg/mL for cyclosporine with $r^2 > 0.99$. Repeatability and reproducibility were <10% CV. Minimal matrix effect was observed. Recovery studies using commercial calibrators to measure specimens prepared from reference materials and dimethyl sulfoxide identified no significant bias for tacrolimus but an average positive bias of 20% for cyclosporine, and a correction factor was used to finalize cyclosporine results for specimens prepared from clinical pharmaceutical products. The positive bias was eliminated when calibrators were prepared in dimethyl sulfoxide.
Conclusions: We have developed and validated a LC-MS/MS method for the measurement of highly concentrated tacrolimus and cyclosporine in specimens prepared from clinical pharmaceutical products. We hypothesize that one or more components in the commercial calibrators have contributed to the positive bias of cyclosporine in those specimens. Our method can be used to support studies that assess nonspecific adsorption by feeding tubes.

P16

A Rare Case of Compound Hemoglobin Lansing/Hemoglobin S Coinherited with Alpha Thalassemia Trait (-Alpha3.7) Presented with Spurious Hypoxemia and Moderate Hemolytic Anemia

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We present a case of a 27-year-old female at 27 weeks of gestation, who presented at the emergency department for vaginal spotting. She was also found to have low oxygenation on pulse oximetry of approximately 82% at room air. Her SpO2 did not improve with O2 supplement. She had a similar presentation a month before, with mild light-headedness and low oxygenation. However, two repeated air blood gas (ABG) findings were normal for oxygen saturation. Hemoglobinopathy was suspected due to the disparity. She was anemic during her presentation, with hemoglobin 8.3 g/dl, RBC count 3.36 million/ul, MCV 81 fl and MCH 24.7 pg. Additional workup showed increased reticulocyte count, decreased haptoglobin, negative direct Coombs test, negative G6PD test, and no evidence of a PNH clone. Capillary hemoglobin electrophoresis showed HbA 59.8%, HbS 34.5%, HbA2 3.6% and a small peak (2.1%) in the Z8 zone with a trailing edge at HbF window. HPLC revealed an “unknown peak” of 8.2% with a retention time of 1.93 minutes as well as the HbS peak. There was also a tiny additional A2 peak unresolved from the main A2 peak. Alpha globin gene sequencing revealed one copy of the -alpha3.7 alpha-globin deletion and one copy of Hb Lansing variant in the alpha2-globin gene. This is consistent with the compound Hemoglobin Lansing/Hemoglobin S coinherited with alpha thalassemia trait. Hemoglobin Lansing is a rare unstable alpha hemoglobin variant with mutation of c.264C>G resulting with a substitution of His by Gln at codon 87. The mutation was first discovered in the alpha 2 gene. Then the same mutation was found in alpha 1 gene later and named as Hemoglobin Lansing-Ramathibodi. To the best of our knowledge, this is the first reported case of Hemoglobin Lansing with alpha thalassemia trait (-alpha3.7) and HbS. Spuriously low pulse oximetry measurements have previously been reported in Hb Lansing variants. It was speculated to be due to different absorption spectra of Hb Lansing which is under study now. The patient also presented with hemolytic anemia. The exact cause was undetermined yet although it might be related to her hemoglobinopathy. Mild hemolytic anemia was reported in two cases of co-inheritance of Lansing-Ramathibodi and Hb Pakse (a non-deletional alpha thalassemia) but not in the members of the same family with Hb Lansing alone. It was also reported that some unstable alpha chain variants, when associated with another alpha thalassemia defect, present with a more severe phenotype including hemolytic anemia even though essentially asymptomatic in a heterozygous state.

P17

Detection of Prostate Cancer Screening Disparities Using Geospatial Analysis of Laboratory Results

Poster 17 was withdrawn.

P18

Comparison of Blood Tubes for Chemistry Analytes Across Three Manufacturers

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As with many aspects of patient care, supply chain shortages over the past few years have caused disruptions to blood collection system inventories across clinical laboratories in the United States. At our institution, this has led to periods where our blood tube inventory had to be supplemented by vendors different from our primary vendors and, increasingly, the use of same tube type from different vendors interchangeably for many tests. Concomitantly, there has been a drive at our institution to reduce blood collection volumes which pose a particular challenge for us given that blood for research purposes is a major component of cumulative draw volume. For those reasons, we compared plasma separator (PST), serum separator (SST), and EDTA tubes from Becton, Dickinson, and Company (BD), Greiner, and Sarstedt. Volumes were 3.5 mL for PST and SST from BD and Greiner, 2 mL for EDTA from BD, and 2.7 mL for all tubes from Sarstedt. Seventy-five volunteers donated blood for this study. A total of 84 chemistry analytes were tested (45 from PST; 34 from SST; and 5 from EDTA tubes) on one of the following instruments: Abbott Architect, Roche Cobas 6000 Analyzer, Diasorin Liason XL Analyzer, and Immulite 2000 xPi. Order of tube draw was randomized and tubes from the same participant were tested at the same time. Statistical analyses included Deming regression for 2-sided comparisons as well as Friedman test. Pertinent findings included biases that were within pre-defined allowable limits for most analytes except for lactate dehydrogenase (LDH) and ammonia which showed biases (%) in two instances (Sarstedt vs. BD) of 19.2% (LDH) and 46.3% (ammonia). These significant differences are likely attributable to an observed increase in hemolysis with the Sarstedt tubes linked to the use of vacuum as opposed to aspiration technique necessitated by the validation design. Additionally, a predominantly, albeit small, negative bias was observed for many analytes when Sarstedt was compared to either BD or Greiner, whereas the bias direction for the BD to Greiner comparison appeared to be random. Our data suggest that tubes from different vendors are essentially interchangeable for some analytes under normal circumstances and can be interchangeable for many analytes under supply shortage conditions. Technique effect on hemolysis should be evaluated and taken into consideration as the rate of hemolysis in low-volume BD and Greiner tubes appears to be lower than that in Sarstedt.

P19

An Organization-wide Analysis of Laboratory Test Cost Variables and Costs as Displayed in the Electronic Health Record: First Steps

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Displaying the cost of laboratory tests and medications in the electronic health record (EHR) at the time of order may influence ordering practices. Our organization's EHR was configured to display a semi-quantitative value adjacent to laboratory orders: "$" tests imply relatively little cost and "$$$$" tests imply resource intensive tests. Cost display is associated with charges from hospital or clinic fee schedules by default but can also be configured to reflect direct laboratory costs. To understand our system's configuration and potentially improve the information being provided to our clinicians upon ordering, all the test ordering data was compiled and analyzed for all individual "orderable" tests within the year of 2021 (Jan 1st 2021 – Dec 31st 2021). Variables analyzed included frequency of test ordering, average test turnaround time, and each of the various possible measures of "cost": direct costs based on labor and reagents/supplies (when available), reimbursement from the Clinical Laboratory Fee Schedule, and pricing from the fee schedule of the largest hospital in our organization (chargemaster). Results showed an extensive rightward skew in each of the "cost" variables, with most routine tests, like the complete blood count (CBC) or complete metabolic panel (CMP), falling in the lower price range and a number of outlier tests with much higher costs (newer forms of molecular testing). There was minimal linearity in correlations between the various price variables. Correlation between chargemaster price by quintile and actual dollar signs displayed in the EHR showed that the two often disagree. No definitive discernable logic was thus identified for the number of dollar signs shown in the EHR based on the possible "cost" variables analyzed here. Between the lab's best estimate for direct costs and chargemaster pricing, a rough correlation with slope greater than 1 was identified, suggesting that chargemaster pricing is systematically higher than the cost of running each test. Between the cost of running each test and reimbursement via the Clinical Laboratory Fee Schedule, a rough correlation with slope less than 1 was identified, suggesting that lab costs are systematically higher than reimbursement. The current lack of strong correlations between these various "cost" variables is helpful as a first step in examining how to improve our organization's EHR system, assessing our laboratory's cost effectiveness, and discussing potential future considerations for hospital chargemaster pricing as well as the US system of reimbursement. Further work is needed to clarify the relationship between cost displays in EHR and physician ordering practices.

P20

Improved Test Utilization After Implementation of a High-sensitivity Cardiac Troponin I: Real-world Experience in a U.S. Emergency Department of an Academic Urban Hospital

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Background: Current guidelines recommend high-sensitivity cardiac troponin (hs-cTn) as the preferred biomarker for diagnosis of acute myocardial infarction. Many U.S. hospitals have recently made or are making the transition to hs-cTn, but questions remain regarding impact on test utilization, operational efficiency, and patient safety. Prior studies evaluating these questions have had methodologic limitations and yielded conflicting results.
Methods: Retrospective observational cohort study of emergency department (ED) patients undergoing cardiac troponin (cTn) testing at two urban hospitals in New York City during the months before and after transition from conventional cardiac troponin I to high-sensitivity cardiac troponin I (hs-cTnI) along with implementation of a 0/2-h diagnostic algorithm for non-ST-elevation myocardial infarction (NSTEMI), at Hospital 1. Hospital 2 served as a control. Primary outcomes included serial (≥ 2) cTn test utilization, probability of hospital admission, and ED length of stay (LOS). The primary safety outcome was, among discharged patients, probability of ED revisit within 72 hours resulting in admission. Results were adjusted for age, sex, temporal trends, and interhospital differences.
Results: At Hospital 1, use of serial cTn tests increased from 18% of encounters to 65% of encounters after hs-cTnI was implemented (adjusted risk difference: 48 percentage points, 95% CI: 45–50, P < 0.001). There was no significant association between intervention and probability of admission (adjusted risk ratio [aRR]: 0.99, 95% CI: 0.89–1.1, P = 0.81) or probability of ED revisit within 72 hours resulting in admission (aRR: 1.1, 95% CI: 0.44–2.9, P = 0.81). The intervention was associated with an increase in average ED LOS (adjusted geometric mean difference: 50 minutes, 95% CI: 50–51, P < 0.001).
Conclusions: Implementation of hs-cTnI, together with a 0/2-h diagnostic algorithm for NSTEMI, was associated with a large improvement in serial cTn testing, neutral effect on probability of hospital admission, and modest increase in average ED LOS.

P21

Impact of CMA on Diagnosis and Clinical Management of Neonates: A Retrospective Single Center Study of a 10-year Cohort

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Introduction: Congenital anomalies are one of the leading causes of mortality in neonatal period. The burden of genetic disease is high in neonates with congenital anomalies. Chromosomal microarray analysis (CMA) is the “first-tier” cytogenetic diagnostic test for individuals with multiple congenital anomalies. The aim of this study is to assess the diagnostic yield and clinical management impact of CMA in a large neonatal cohort over a 10-year period at a single medical center.
Methods: This is a retrospective study of a cohort of neonates tested by CMA at UVA Cytogenetics Laboratory between the years of 2013-2022. All individuals had either an isolated (major) congenital anomaly (CA) or multiple congenital malformations (MCA). We evaluated the diagnostic yield of the CMA in this neonate cohort and the frequency of positive CMA findings for specific phenotypes, as well as impact of CMA findings in the clinical management of patients.
Results: Of the 965 patients analyzed, 656 (68%) had normal results, 166 (17%) patients only had variants of uncertain significance (VUS), 128 (13%) patients had pathogenic alterations (thus confirmed genetic diagnosis), and 15 (2%) patients only had absence of heterozygosity (AOH) regions meeting our reporting criteria. Further details on presence of specific CNVs in the cohort and, positivity per presence/absence of multiple and specific anomalies is still ongoing and will be given in the presentation. For patients received a genetic diagnosis through CMA analysis, genetic findings were considered beneficial for clinical management, and a direct change to medical management occurred.
Conclusions: In this study, we found that the overall diagnostic yield for CMA in this neonate cohort is at approximately 13%. The confirmed genetic diagnosis affected the clinical management/treatment plan of this subset of neonatal patients. While first-tier testing for MCA and other indications is increasingly moving to ES/GS approaches, CMA continues to offer diagnostic and actionable genetic information in a timely matter. Overall, the implementation of CMA to a neonatal cohort at our center has increased the proportion of patients receiving a confirmed genetic diagnosis and affected the management/treatment plan of a subset of neonatal patients.

P22

Platelet Inhibition Testing: Whole Blood Point-of-care vs Traditional Platelet Aggregometry

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Monitoring drug response to ensure optimal platelet suppression is necessary in select patients on dual antiplatelet therapy (DAPT). At our institution, responses to aspirin (ASA) and P2Y12 inhibitors (P2Y12-Is) are assessed by light transmission aggregometry (LTA) using the Helena AggRAM assay. This method requires platelet-rich plasma (PRP) and is labor intensive. Platelet mapping using thromboelastography (TEG) is an alternate method, which offers point-of-care testing on whole blood. Here, we aimed to evaluate the concordance of our LTA assay with TEG, as well as the VerifyNow® PRUTest. We aimed to run testing on at least 20 patient samples; however, at the time of abstract submission, only 10 samples were available. Ten blood samples from 8 patients on dual anti-platelet therapy were collected in preparation for neurologic stent placement. Prepared PRP was analyzed by LTA on the Helena AggRAM assay. The maximal amplitude of the aggregation curves was recorded in the presence of high dose (HD) ADP, low dose (LD) ADP, and arachidonic acid (AA). Whole blood was analyzed by TEG using PlateletMapping ADP & AA assay cartridges on the Haemonetics® TEG 6s analyzer, and by the VerifyNow® PRUTest. Thresholds to qualify platelet suppression as optimal or suboptimal were defined a priori following established guidelines. Concordance between methods was calculated using the following formula: (optimal/optimal + suboptimal/suboptimal) / total number of samples. Pearson correlation between units of measure was also determined. For P2Y12-I response, concordance between LTA and TEG was 70% (correlation was r = 0.76 between TEG and LTA with HD ADP, and r = 0.70 between TEG and LTA with LD ADP). Concordance between VerifyNow® and LTA was 60% (correlation was r = 0.84 between VerifyNow® and LTA with HD ADP, and r = 0.78 between VerifyNow® and LTA with LD ADP). Finally, concordance between VerifyNow® and TEG was 30% (correlation was r = 0.81). Regarding ASA response, concordance was 80% between LTA and TEG (correlation was r = 0.31). To summarize, overall concordance ranged from 30 to 80% across platforms. For P2Y12 inhibition, results obtained from LTA with HD ADP and VerifyNow® had the strongest correlation (r = 0.84). Interestingly, the correlation between VerifyNow® and TEG was similarly elevated (r = 0.81), but concordance was poor (30%). When comparing TEG to LTA, the strongest correlation was between LTA with HD ADP and TEG (r value = 0.76). Concerning ASA inhibition, concordance between LTA and TEG was acceptable; however, correlation was weak (80%; r = 0.31). Results from this preliminary study support the potential use of TEG to monitor platelet response to therapy. We plan to continue our testing to include a minimum of 20 samples, and also consider patient outcomes, before implementing any laboratory workflow changes.

P23

Bone Marrow Differential Cell Count Uncertainty in the Classification of Plasma Cell Neoplasms

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Pathologic evaluation of bone marrow is diagnostically essential for many hematologic diseases, with quantification of cellular composition an important step in the pathologic work-up. Many diagnostic criteria for hematologic diseases contain precise cellular thresholds, for example 10% and 60% plasma cells in plasma cell neoplasms (PCN). Therefore, accurate cellular quantification is necessary, as it impacts treatment decisions. This process is typically performed manually and is subject to errors, including interoperator variability and heterogeneity of cellular composition within the aspirate smears. Rumke statistics were developed to predict errors in manual quantification of hematologic specimens, with resulting statistical confidence intervals. We set out to determine how statistical uncertainty of plasma cell percentages from manual differential counts could potentially affect the diagnosis and classification of PCN. Here, we extracted from the EMR a large data set containing pathologic diagnoses and laboratory data for 16,737 cases of PCN. Using the R programming language, we developed an automated method to extract plasma cell percentages from unstructured text containing manual bone marrow differential counts. Differential cell counts with plasma cell percentages were available for 4,523 cases, of which 2,445 were initial cases in the data set. Rumke statistics were calculated for each initial case using the Clopper-Pearson 95% confidence interval. Next, we identified cases where the plasma cell Rumke intervals encompassed the 10% or 60% threshold, thereby potentially changing diagnostic categorization. Of the initial cases, 228 (9.3%) encompassed a threshold (204 at 10% and 24 at 60%). To determine if diagnostic categorization would be affected, we screened for databased myeloma defining events (MDE) - hemoglobin (<10 g/dL), serum creatinine (>2 mg/dL), and total calcium (>11 mg/dL). At the 10% plasma cell threshold, 50 cases had one or more laboratory MDE and 127 had none. In cases with MDE, crossing the 10% threshold meets criteria for plasma cell myeloma (PCM) and below would likely lead to further work-up, including diagnostic imaging. In cases with no MDE, crossing the 10% threshold changes the diagnostic categorization from monoclonal gammopathy of undetermined significance to smoldering myeloma. In our data set, cases that straddled the 60% threshold all met criteria for PCM, whether they crossed the 60% threshold or not. These findings show that differential cell counts close to diagnostic thresholds fall within error ranges in a significant number of cases of PCN and potentially change diagnostic categorization. Such uncertainty must be appreciated and taken into consideration when categorizing a patient's disease. This work also highlights the need to develop more accurate and representative methods to generate differential cell counts, such as automated methods from whole slide digital images. In addition, our methods highlight the utility of using R software to extract meaningful data from unstructured free text at large scale.

P24

The Million Patient Labset: A Large, De-identified Dataset of Longitudinal Clinical Laboratory Results from One Million Patients

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Laboratory testing is integral to the diagnosis and treatment of disease. Advances in electronic medical records and computation have initiated an era of 'big data' for laboratory medicine. However, most health data continues to exist in isolated and inaccessible information silos, limiting public utility. To address this gap, we have developed a large, de-identified, longitudinal dataset of laboratory results from over one million patients, called the Million Patient Labset (MPL), which is free and open to the public. The MPL was produced from the combination of two large healthcare systems with IRB and information security approvals. It includes 1,112,550 patients from across 1,920 healthcare sites in two states from 2017 through 2021, with 4,404 different clinical assays represented. Sites included primary care clinics, secondary care facilities for dialysis, infusions, rehabilitation, and other subspecialties, and tertiary centers for major surgery, trauma care, cancer care, and other complex medical services. Assays having fewer than 100 results were excluded. Limited patient demographic and encounter metadata are also included. Protected health information was de-identified in accordance with Health Insurance Portability and Accountability Act of 1996 (HIPAA) safe harbor standards. Service dates and times were altered to obscure absolute timestamps, while approximately preserving interval lengths between test results of the same patient, and general age and time of testing averages across patients. Time of day, day of week, and seasonality were approximately preserved. Data were validated through randomly selected comparisons against the original patient records, prior to destroying re-identification keys. In conclusion, we have produced a large de-identified open-access dataset of clinical laboratory results from over one million real patients. We hope this resource will be valuable for researchers exploring human clinical variation, medical artificial intelligence, reference interval optimization, and other data-driven studies.

P25

Delayed Hemolytic Transfusion Reactions Could be Prevented by a National Alloimmunization Registry

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Evanescence of alloantibodies to RBC antigens places patients at risk of delayed hemolytic transfusion reactions (DHTRs) unless the transfusion service is aware of their alloantibody history. In the past year, three patients with sickle cell disease (SCD) developed a DHTR at our institution because their pre-transfusion testing did not reflect their full alloimmunization. We sought to determine how often the pre-transfusion antibody screen is negative or fails to show the full alloimmunization profile. We reviewed the electronic records of all current adult patients with SCD receiving chronic outpatient RBC transfusions (including red cell exchange) to collect demographic and laboratory results to answer this question. Our analysis included 162 patients of African-American descent: 80 (49%) males and 82 (51%) females, with an average age of 34 years. The majority, 92 or 56%, had a history of alloimmunization with a mean number of 3 antibodies (range: 1-10). The most common were to the C, E, and K antigens. The next two most common alloantibodies were nonspecific, representing alloimmunization to an antigen that could not be further determined, followed by the D antigen. In 81 patients, the most recent antibody screen did not reflect their history, with most being completely negative (n=69), and the rest (n=12) unable to detect all alloantibodies of which they had a history. The antibodies most often undetectable were: Anti-E, Anti-C, and Anti-D. These are simultaneously the second, first, and fifth most common antibodies in this population, all of which are considered clinically significant and capable of causing a hemolytic transfusion reaction. Of note, the alloantibodies implicated in the recent DHTRs we observed, were to the JK^a, Jk^b, Fy^a and the S antigens. In addition, 28 individuals (17% of the total) had at least one antibody to a low incidence antigen (LIA) such as Go^a, V, Vs, Js^a, Kp^a and Lu^a. Five (3%) patients were exclusively sensitized to one or more low incidence antigens. Considering that commercially available reagent red cells utilized to perform pre-transfusion testing may lack LIAs, knowing the history of alloimmunization is the only way to prevent hemolytic reactions. In conclusion, evanescence and limitations of the commercially available reagents to test patients with SCD prior to a transfusion place them at increased risk of transfusion reactions. One potential way to minimize risk from the latter is to perform serologic crossmatching of all units intended for patients with SCD, independent of the result of the antibody screen. This is the practice we have instituted several years ago in our transfusion service. However, the solution to both problems is a national repository of alloimmunization histories accessible to all transfusion services. Such informatics tools would help avoid DHTRs in patients with and without SCD.

P26

Monitoring Infected Reticulocytes During Murine Malaria Infection

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Malaria infection is a major cause of mortality worldwide. According to the 2022 World Health Organization Malaria Report, malaria caused approximately 247 million infections and 619,000 deaths in 2021, with more than 470,000 children dying of malaria. The gold-standard for measuring parasitemia is counting infected red blood cells (RBCs) by eye using Giemsa staining whole blood smears. This method is time consuming and is subject to error by both who is counting, the number of cells counted, and which frames are selected for counting. Automating the process of measuring malaria infection by flow cytometry decreases both the time required to obtain accurate parasitemia counts and the possible error on behalf of the researcher. Hundreds of thousands of cells can be counted by flow cytometry in a shorter period of time. Animal models of malaria infection are widespread and well-characterized. The rodent malaria strain *P. berghei* has shown preferential infection of reticulocytes over mature RBCs. Here we outline a method of measuring *P. berghei* blood stage infection in reticulocytes and mature RBCs and comparing the results to Giemsa stained whole blood smears. Using commercially available *P. berghei* ANKA expressing green-fluorescent protein (GFP), we infected wild type mice with $1x10^6$ parasitized RBCs by intraperitoneal injection. Whole blood samples were collected daily starting day 3 post infection through day 7 by tail vein collection. Random and representative fields of Giemsa stained peripheral smears were selected to measure the percentage of parasitemia in mature RBCs and reticulocytes for a total cell count of approximately 1000. For flow cytometry, whole blood was incubated in 500uL of 1X SYBR Green I Nucleic Acid Gel Stain in PBS at 37°C for 20 minutes in the dark, washed with PBS, and stained with anti-CD71 to label reticulocytes. During the early stages of infection, the reticulocyte percentage of infected animals is not significant from uninfected animals, approximately 1.86%. As parasitemia increases over time, although the percentage of total reticulocytes decreases, the percentage of infected reticulocytes increases. On day 3 through 7 for one experimental replicate, day 3 demonstrated 1.86% total reticulocytes, and of these 2.56% reticulocytes were infected; day 4 had 0.66% total reticulocytes, and of these 32.92% were infected; day 5 showed 0.18% reticulocytes with 71.81% infected reticulocytes; on day 6 there were 0.04% reticulocytes with 75.44% infected reticulocytes; and day 7 had 0.01% reticulocytes with 69.56% infected reticulocytes. There was a strong correlation (R^2 = 0.9147) when comparing flow cytometry to measure parasitemia with counting parasitemia by peripheral smear. This flow cytometry panel is an excellent tool to assess malarial infection of reticulocytes compared to mature RBCs and can be applied to other malarial species while decreasing bias, error and time needed to conduct the experiment.

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