

**CLINICAL CHEMISTRY
& IMMUNO ASSAY:
FROM BENCH
TO BEDSIDE**

22 NOVEMBER 2019

MESSAGE FROM THE CHAIR:

It is a great honour to serve as the first chair of the AACC India Section. The AACC India Section was established as a first international pilot project of the American Association for Clinical Chemistry (AACC), in 2018. Its objective is to connect with global leaders in clinical chemistry, molecular diagnostics, mass spectrometry, translational medicine, laboratory management and other frontier areas of laboratory medicine.

AACC India Section activities have included:

- i) granting 30 AACC trainee memberships to postgraduates in India
- ii) organizing two symposiums, in conjunction with national conferences in Goa & New Delhi, in 2018
- iii) holding an AACC India Section event in January 2019 at AIIMS, New Delhi with international and national speakers, and clinicians.

AACC India Section held a meet and greet event at the 71st AACC Annual Scientific Meeting & Clinical Lab Expo on 7th August in Anaheim, California, US. The successful meet and greet session returns to our CME on 22nd November, 2019 in Kokilaben Dhirubhai Ambani Hospital & Medical Research Institute in Mumbai with Dr. Carmen L. Wiley, AACC President and other esteemed international and national faculty. We have seven outstanding international speakers along with Dr. Wiley who are attending the event. The speakers include laboratory experts, clinical chemists, management experts, accreditation authorities and IVD specialists. During the event, we are also felicitating mentors of Clinical Chemistry and Laboratory Medicine. This well received event is sponsored by 9 IVD manufacturers, among which Platinum sponsors are: i) Abbott Diagnostics, ii) Agappe, iii) Transasia; Gold sponsors are i) Sysmex and ii) Roche Diagnostics; Silver sponsors are: i) Beckman Coulter, ii) Horiba Medical, iii) Ortho Clinical Diagnostics and iv) Siemens Healthineers.

During the event, we will be launching an AACC India Section travel grant in the amount of one lakh INR to attend the AACC Annual Scientific Meeting & Clinical Lab Expo in Chicago 2020 for a young post graduate student. In addition, the Section is introducing one AACC India Section Fellowship Training (one lakh INR) and two Educational Grants (50,000 INR each) for training and projects that are based on an Indian perspective. The selection process for the grants will be done by an international expert panel from AACC.

With our distinguished executive committee members, we expect another great year for the AACC India Section and our valued members.

Bio of Chair, AACC India Section



DR. BARNALI DAS

Dr. Barnali Das, MBBS, MD, DNB & PGDHHM, is a Consultant in Biochemistry & Immunology division of Kokilaben Dhirubhai Ambani Hospital & Medical Research Institute, Mumbai. She is an Executive Member of the Scientific Division, International Federation of Clinical Chemistry & Laboratory Medicine (IFCC). She also served as a Member of the IFCC Committee for Standardization of Thyroid Function Tests (IFCC S-CTFT), 2011-2017. She is also a Corresponding Member, IFCC Committee for Reference Interval & Decision Limit. She has been honored with an adjunct faculty position in Kasturba Medical College, Manipal, MAHE. She is a College of American Pathologist (CAP) Inspector & NABL Assessor.

Dr. Barnali is a recipient of two oration awards and four international and seven national awards from American Association of Clinical Chemistry (AACC Outstanding Speaker Award), International Federation of Clinical Chemistry & Laboratory Medicine (IFCC Development of Quality Competence in Medical Laboratories- DQMCL Award), College of American Pathologist (CAP Inspector Excellence Honour for the year 2018), Asia Pacific Federation of Clinical Biochemistry (APFCB Young Scientist Scholarship), Reliance Group Corporate Social Responsibility (The Woman of Substance Award), Association of Clinical Biochemists of India (Dr. T. N. Pattabhiraman Oration Award, Pitabus Jamuna Burma Memorial Award and Dr. C. Sita Devi Award) and Association of Medical Biochemists of India (Dr. Ajit Singh Saini Oration Award and also Brig. Ramesh Sinha Memorial Certificate & Gold Medal from Association of Medical Biochemists of India). This year, she is recipient of 2019 "Diagnostic Leadership Award in Achiever Category" from Indian Express Group, MT India 2019 "Healthcare Leader in Quality & Management" in Voice of Healthcare and 2019 Zee Business National Healthcare Leadership Award in 'Woman Leadership Category'. Her biography has been featured in a book named "And So Can You" (where 17 successful doctors share their inspiring stories).

Currently she is serving as Chair, AACC India Section. She can be reached at the following email address: drbarnalid@gmail.com.

AACC India Section CME
Clinical Chemistry & Immunoassay
22 November 2019

Keynote Address by Dr. Carmen L. Wiley, AACC President
Immunoassay Interferences and Challenges



DR. CARMEN WILEY

Immunoassays are the workhorses of clinical laboratories. Using antibodies for diagnostic measurements provides high specificity and sensitivity. Despite all the successful uses of immunoassays, there are still problems with interferences. In this talk I review how the common immunoassay formats work. I cover the double antibody sandwich assays, competitive inhibition assays, and delayed capture assays. I then review how the different types of interference mechanisms cause falsely elevated and suppressed results for each assay format (i.e. steric hindrance, bridging, etc.). Finally, I review current strategies to troubleshoot interference.

Learning objectives:

After completing this activity, the learner will be able to:

1. List the common interferences that impact immunoassay results
2. Describe how interferences impact patient results
3. Create a plan for mitigating these interferences

Brief Bio of AACC President:

Dr. Wiley is the President of AACC, a global scientific and medical professional organization dedicated to better health through laboratory medicine. Dr. Wiley is also the Chief Medical Officer of start-up company, Veravas, and a Clinical Laboratory Affairs and Innovation Leader in Spokane, WA. She has a Bachelor's degree in Chemistry from the University of Minnesota, a Master's degree in Organic Chemistry from the University of Washington, a Doctoral degree in Organic Chemistry from the University of Washington, and was a COMACC Accredited Fellow at the Mayo School of Medicine. She is board certified by American Board of Clinical Chemistry (ABCC) and a Fellow of the Academy of the American Association of Clinical Chemistry (FAACC).

She was a Regional Manager of Scientific Affairs – Cardiac at Roche Diagnostics. In this role, she was responsible for leading and developing the Medical & Scientific Liaisons in their relationships with the medical/scientific community, with the objective of critical scientific exchange including medical/scientific education. She played a key role in providing support to healthcare professionals as well as internal Roche scientific groups and local business teams.

Previously, she was the Scientific Director at PAML where she was responsible for the medical and scientific oversight of all laboratory testing and oversaw all aspects of PAML's research and development program. Previously, she was Co-Director of Chemistry, Immunology and Point of Care at Providence Health and Services, Sacred Heart Hospital in Spokane, WA and the Head of Clinical Chemistry in the Division of Laboratory Medicine and Pathology at the Marshfield Clinic in Marshfield, WI.

Total Lab Automation in Clinical Chemistry Laboratory

Dr. Qing Meng



DR. QING MENG

Clinical laboratories are facing the challenges of staff shortages, increasing test volume, improvement of testing quality and turnaround time, space constraint, and workflow improvement. With these challenges, one of the major advances in clinical laboratories is the total laboratory automation. Total laboratory automation (TLA) systems fully integrates modular systems, workstations, and bioinformatics throughout the pre-analytical, analytical, and post-analytical processes. This talk will identify the steps and process in implementation of automation with integration of informatics and involvement of workflow analysis, configuration, consolidation, connection, interfacing, testing, and validation. I will also discuss the challenges and solution in certain scenarios and key bottlenecks. At the end, participants will learn the benefits and be able to identify opportunities in implementation of total laboratory automation.

Learning objectives:

After completing this activity, the participants will be able to:

1. Understand the principle, process, steps, and benefits of implementation of total laboratory automation (TLA)
2. Describe the challenges and solutions in implementation of TLA
3. Identify opportunities for TLA to sustain continuous laboratory performance and quality improvement

Speaker Bio: Dr. Meng is Professor and Section Chief of Clinical Chemistry Laboratories, Department of Laboratory Medicine at The University of Texas MD Anderson Cancer Center. His research interests include tumor biology, tumor biomarkers, and cancer diagnostics. He has published over 130 peer-reviewed papers with H-index of 27. Dr. Meng has served the professional associations and organization in numerous capacities including IFCC Committee on Analytical Quality (C-AQ).

Tumour Markers: Challenges in Standardization and Assays:

Dr. Lakshmi Ramanathan



DR. LAKSHMI RAMANATHAN

Biomarker analysis plays an essential role in cancer. This session will focus on current technologies and challenges in the standardization as well as determination of tumor markers. Traditional as well as new technologies that are used along with limitations of immunoassay methodologies will be discussed. PSA and bhCG methodologies and limitations will be explained in the clinical context with specific case discussion.

Learning Objectives:

1. Review use of cancer markers
2. Explain methodology/interferences/limitations, specific cases
3. Describe challenges in tumor markers and biomarkers standardization

Speaker Bio:

Dr. Ramanathan is the Service Chief of Clinical Chemistry in the Department of Laboratory Medicine at Memorial Sloan Kettering Cancer Center in New York City. She obtained her PhD in Nutritional biochemistry and Metabolism at Massachusetts Institute of Technology in Cambridge, Massachusetts, USA. Her research interests include laboratory automation and biomarkers in cancer diagnostics. She is very active in AACC and is the present chair of the Science Practice and Core Committee of AACC and was the past chair of the New York Metro Local Section.

Standardizing LCMS/MS Assays and Method Validation

Dr. Ravinder J. Singh



DR. RAVINDER SINGH

Immunoassays have been the methodology of choice for the analysis of steroids and amines in making diagnosis of patients affected with Cushing's, pheochromocytoma and congenital adrenal hyperplasia (CAH). But very often the results from the endocrine laboratory had to be repeated with the HPLC-extraction assays to rule out the possible cross reactivities of the glucocorticoids, steroid metabolites and drugs with the antibody detecting the analyte. In the past the use of gold standard MS technology in the clinical diagnostic labs have been limited because of labor intensive extraction, sample preparations and chromatographic separations. Recently the use of MS/MS (tandem MS) technology in liquid and gas chromatography has revolutionized the application of MS technology in clinical laboratories. This is due to reduction in effort for extraction and chromatography and as a result has a scope for expediting the analysis of steroids, biogenic amines and peptides for the diagnosis of various endocrine disorders. We at Mayo have implemented this technology for the routine analysis of steroids, biogenic amines and peptides. These methods not only provide reliable results for endocrine disorders but also can be used as reference methods by other laboratories and accreditation agencies. Until recently most of the phenotypic information on congenital endocrine disorders have relied on biochemical testing of steroids, biogenic amines and peptides but is now being combined with the molecular testing. In spite of the mutational analysis of endocrine disorders the correlation of the phenotype relies more on biochemical testing than the molecular testing.

Learning Objectives:

After completing this activity, the learner will be able to:

1. List the challenges that exist in standardizing LC-MS/MS hormone assays
2. Identify approaches to establishing standardization between LC-MS/MS methods
3. Discuss how standardization of LC-MS/MS methods has a positive impact on patient care

Speaker Bio: Ravinder J. Singh, PhD, is the Director of the Mayo Clinic Endocrine Laboratory. He has a focused area of investigation that has broad applicability to the field. Dr. Singh studies the application of liquid chromatography-tandem mass spectrometry (LC-MS/MS) to clinical laboratory analysis. Many of the methods that Dr. Singh developed are now considered reference methods. They have subsequently been utilized for method standardization efforts as well as to establish clinical disease correlates, which he has published with his collaborators. He is co-primary investigator, one industry-funded and two NIH-funded grants and the co-director, Immunochemical Core Laboratory, Mayo Clinic. Dr. Singh received the Clinical and Translational Science Award for novel methodology, National Center for Advancing Translational Sciences, National Institutes of Health. He was the former chair, Midwest Local Section, (AACC) and the former Director, Clinical Chemistry Postdoctoral Fellowship, Mayo Clinic

Therapeutic Drug Monitoring using Oral Fluid

Dr. Amitava Dasgupta



DR. AMITAVA DASGUPTA

There are over 4,000 drugs but most drugs have wide safety of margin and do not require therapeutic drug monitoring. However, approximately 26 drugs require therapeutic drug monitoring due to narrow therapeutic window and better correlation between serum/whole blood drug levels and therapeutic efficacy/toxicity compared to dosage and clinical response. Therapy with another 25-30 drugs may also get benefits from therapeutic drug monitoring. Usually plasma/serum is used for therapeutic drug monitoring for most drugs except immunosuppressants (cyclosporine, tacrolimus, sirolimus and everolimus) where monitoring is conducted in whole blood. However, collecting blood is invasive especially in pediatric patients. Therefore, oral fluid (saliva) is gaining acceptance as an alternative specimen for therapeutic drug monitoring. Oral fluid is an ultrafiltrate of blood where drug concentration approximately represents unbound (free) drug level in serum. Although basic and neutral drugs are diffused passively in oral fluid, some drugs are actively transported in saliva and other drugs are found in extremely low concentration with no correlation with serum drug levels. As a result, not all drugs can be monitored using oral fluid. Common drugs monitored in oral fluid are classical anticonvulsants (phenytoin, carbamazepine, ethosuximide, and phenobarbital), digoxin, primidone, quinidine, theophylline, caffeine (in neonates), lithium and methotrexate. More recently, monitoring of lamotrigine and mycophenolic acid in oral fluid have been reported. Currently, FDA approved devices are available for collecting oral fluid. However, drug levels in oral fluid must be interpreted carefully due to lack of available reference ranges for some drugs.

Learning objectives:

1. Gain competence on using oral fluid for therapeutic drug monitoring (TDM)
2. Familiar with technical challenges using oral fluid for TDM
3. Familiar with drugs that can be monitored using oral fluid
4. Implement TDM using oral fluid in their laboratories

Speaker Bio: Dr. Amitava Dasgupta received his PhD in chemistry from Stanford University and completed his fellowship training in Clinical Chemistry from the Department of Laboratory Medicine at the University of Washington School of Medicine at Seattle. He is board certified in both Toxicology and Clinical Chemistry by the American Board of Clinical Chemistry. Currently, he is a tenured Full Professor of Pathology and Laboratory Medicine at the University of Texas McGovern Medical School at Houston and the Director of Clinical Chemistry and Toxicology Laboratory of Memorial-Hermann Laboratory Services. Dr. Dasgupta's major focus of research is in the field of toxicology and therapeutic drug monitoring. He has published 230 scientific papers, wrote many invited review articles and abstracts edited, co-edited, co-authored and wrote a total of 20 books. He is on the Editorial Board of six journals. He is the recipient of the 2009 Irvine Sunshine Award from the International Association for Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT) for outstanding contribution in clinical toxicology and in 2010 he received the AACC Outstanding contribution to education Award.

Harmonization of Pediatric Laboratory Testing: Is it something different

Dr. Khushbu Patel



DR. KHUSHBU PATEL

Harmonization in laboratory medicine requires attention to the total testing process from pre-analytical to post-analytical factors. Failures in any stage of the testing process can negatively impact the quality of test results and lead to adverse patient outcomes. Pediatric laboratory medicine has its own unique challenges when it comes to harmonization. Unique pre-analytical factors in this patient population can influence both the analytical and post-analytical stages of testing. Furthermore, accurate interpretation of laboratory data requires age and sex specific reference intervals. This session will discuss the pre-analytical challenges associated with low samples volumes. Examples of strategies used to harmonize laboratory test results across a pediatric hospital system will be provided in this presentation. Lastly, this session will focus on informatics approaches and other resources used in implementing pediatric reference intervals.

Learning Objectives:

1. List pre-analytical and analytical factors unique to pediatric populations and their impact on laboratory testing
2. Discuss how to overcome operational challenges in harmonizing patient laboratory data across a pediatric health system
3. Identify approaches to establishing and verifying pediatric reference intervals

Speaker Bio: Khushbu Patel, PhD is an Assistant Professor of Pathology at UT Southwestern and the Associate Clinical Director of clinical chemistry and mass spectrometry laboratory at Children's Health of Dallas. Her research interests include using metabolic and proteomic approaches for development of novel biomarkers for pediatric disorders. She is an active member of AACC serving on the SYCL core committee and organizing committee for AACC's Annual Disruptive Technology Competition. She also is a member of College of American Pathologists Instrumentation Committee.

Biological Variation: Improved Interpretation of Lab Results and Reduced False Rejections for QC

Dr. Joe M. El-Khoury



DR. JOE EL-KHOURY

Biological variation is the inherent variability in analyte concentrations within an individual and across individuals over time. This analyte-specific information can be used to set analytical quality specifications, designing quality control programs and defining reference change values. However, studies that established biological variation data for common laboratory analytes are old and produced conflicting results, making them not reliable for clinical use. In this session, will review the current and potential uses of biological variation and discuss reliable sources for retrieving accurate biological variation data.

After this session, the learners will be able to:

1. Define biological variation
2. Describe how biological variation can help reduce false rejections of QC
3. List reliable sources for biological variation data

Speaker Bio: Dr. Joe El-Khoury is an Assistant Professor of Laboratory Medicine at Yale University and Director of Clinical Chemistry at Yale-New Haven Health. He is board certified by the American Board of Clinical Chemistry and a Fellow of the AACC Academy. Dr. El-Khoury also serves on the SYCL Core Committee, AACC-Middle East Scientific Committee, 2021

AACC Annual Meeting Organizing Committee and is Chair-Elect for the New York-Metro Local Section.

External Quality Assurance and Proficiency Testing

Dr. Robert Rej



Proficiency testing (PT) and external quality assurance (EQA) comprise a broad range of applications including providing participants and public health authorities with estimates of measurement uncertainty and national infrastructure; providing education; provision of a practical basis for accreditation and regulatory compliance. All branches of medical laboratory science have employed external quality assurance as a basis for improvement and comparability. The opportunities and challenges reviewed include: the proper establishment of multiple target values in comparison to a system of traceability to reference or definitive methods; continuous review of EQA data to examine bias and/or trends; the problems of matrix effects and commutability of patient and proficiency test samples; generating information on laboratory infrastructure and trends in analytical technique and performance; providing education and setting goals for laboratory improvement; the role of programs in legal mandates and accreditation.

Speaker Bio: Robert Rej, Ph.D. is Associate Professor of Biomedical Sciences at the State University of New York at Albany, School of Public Health and has served as Director of Clinical Chemistry and Hematology at the Wadsworth Center for Laboratories and Research of the New York State Department of Health. He is currently a member of the Board of Editors for Clinical Chemistry and The Journal of Medical Biochemistry and has also served on the Editorial Boards of several other journals including Clinica Chimica Acta. He has authored more than 100 papers and book chapters, many devoted to issues of laboratory quality and accreditation. He has served as member and chair of several committees and subcommittees for CLSI, AACC, IFCC, APHL, and has served as chair of the US delegation to ISO Technical Committee 212 on medical laboratory testing and in-vitro diagnostic test systems. Dr. Rej has testified before the U.S. Congress on laboratory issues and was a member of Clinical Chemistry and Toxicology Devices Advisory Panel to the US FDA. He has lectured extensively throughout the Americas, Europe, Australia, and Asia.

Introduction of the Office Bearers of the AACC India Section:

- Chair: Dr. Barnali Das, Consultant, Laboratory Medicine, Kokilaben Dhirubhai Ambani Institute, Mumbai
- Chair Elect: Dr. Asmita Hazra, Head, Dept. of Biochemistry, Pali Govt Medical College, Rajasthan.
- Secretary: Dr. Sudip Kumar Datta, Assistant Professor, Dept. of Lab Medicine, AIIMS, Delhi
- Treasurer: Dr. Mrinalini S Patwardhan, Biochemist, Dr. Patwardhan's Pathology Laboratory, Mumbai
- Program Chair: Dr. Saswati Das, Specialist Biochemistry, Dr. Ram Manohar Lohia Hospital & AVBIMS, IP University

Local Scientific Committee:

- Dr. Kannan Vaidyanathan, Professor, Department of Biochemistry & Deputy Medical Superintendent & Scientist, Pushpagiri Research Center, Pushpagiri Institute of Medical Science & Research Centre
- Dr. Vanita Lal, Professor & HOD, Department of Biochemistry, GIMS, Noida
- Dr. Arnab Pal Additional Professor, Department of Biochemistry, PGIMER, Chandigarh
- Dr. Srinivas Gowda, Assistant Professor, Department of Biochemistry, MAMC, University of Delhi

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AACC
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