Welcome to the CSCC Conference 2014

The 58th Annual Conference of the Canadian Society of Clinical Chemists

"Clinical Chemistry: A bridge to better healthcare""

Held under the auspices of

This event is an Accredited Group Learning Activity as defined by the Maintenance of Certification Program of the CSCC/CACB Professional Development Program.

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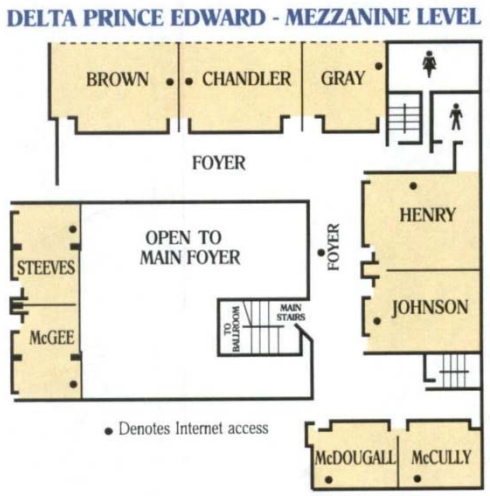
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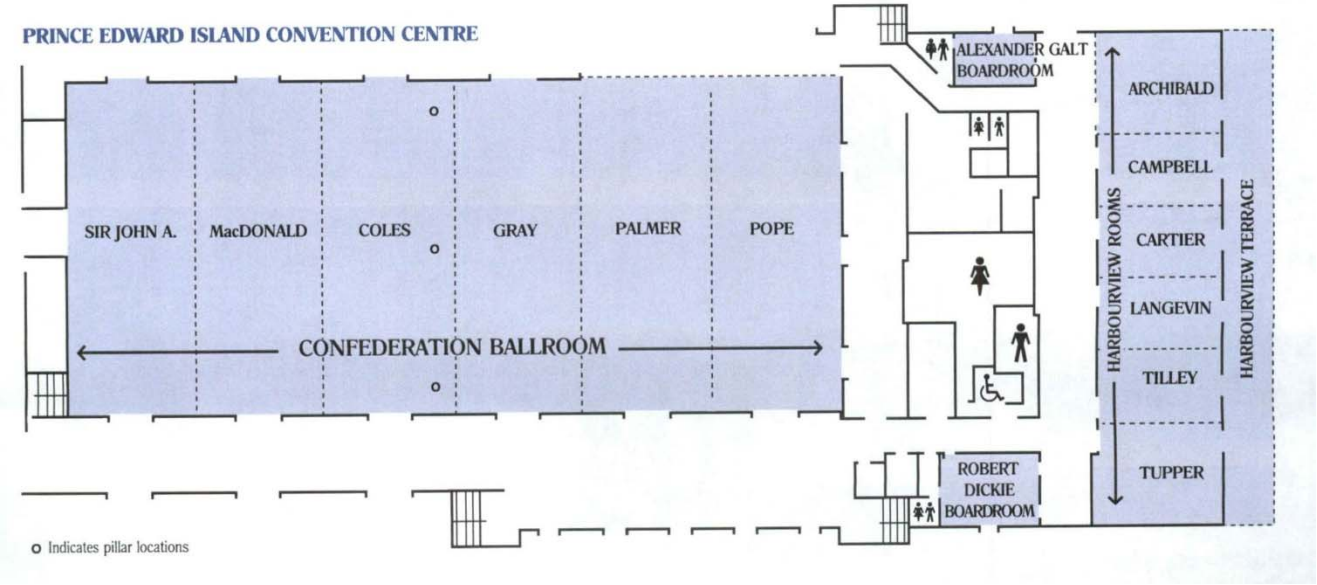
PRINCE EDWARD ISLAND CONVENTION CENTRE
ALEXANDER GALT
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SIR JOHN A.
MacDONALD
COLES
GRAY
PALMER
POPE
CONFEDERATION BALLROOM
ROBERT
DICKIE
BOARDROOM
Indicates pillar locations

CSCC 2014
58th Annual Meeting

June 8-11, 2014
Delta Prince Edward Hotel
PEI Conference Centre
Charlottetown PE

Head Office
4 Cataraqui Street
Suite 310
Kingston ON K7K 1Z7
Tel 613.531.8899
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office@cscc.ca
Web Site: www.cscc.ca

Dear Colleagues,

It is my pleasure to welcome you to the 58th Annual Meeting of the Canadian Society of Clinical Chemists/la Société canadienne des clinico-chimistes in the beautiful city of Charlottetown, Prince Edward Island. This is the first time that we have held our annual meeting in this historic city, the "Birthplace of Confederation" and it is a visit that is long overdue.

Inspired by the famous Confederation Bridge, the theme of this year's meeting is, "Clinical Chemistry: A bridge to better health." The organizing committee has developed a stimulating scientific program and exciting social activities that promise an educational and memorable experience for all. The scientific program includes a keynote address, "Adding Value to Laboratory Medicine", by Dr. Graham Beastall, President of the IFCC, and symposia on Laboratory Utilization, Molecular Diagnostics, Pediatric Care and Men's Health. Together with workshops, roundtables, posters and the latest in technology exhibits, this year's conference promises to educate and inform you. A special event this year is the Charity Run/Walk, an opportunity to get some exercise with fellow biochemists and support a worthwhile local charity.

While in Charlottetown and Prince Edward Island, I hope that all of you will take advantage of the wonderful sights and activities that this special part of Canada has to offer; a place of historic charm featuring breathtaking seascapes, pastoral countrysides, unique shops and restaurants and friendly hospitable "kindred spirits".

Have an enjoyable and productive meeting in beautiful Charlottetown.

Best wishes,

David W. Kinniburgh PhD., FCACB
President, Canadian Society of Clinical Chemists

Program Overview

Friday June 6		
0800-1730	CACB Oral Exams	McCully
Saturday June 7		
0800-1700	CSCC Council	Chandler
0800-0900	Council breakfast & lunch	Brown
0800-1400	CACB Oral Exams	McCully
1200-1700	Registration	Confederation Foyer
1400-1700	CACB Board of Directors	J.H. Gray
Sunday June 8		
0730-1700	Registration	Confederation Foyer
0730-0900	Annual Meetings Committee	Robert Dickie
0800-1230	CACB Oral Exams	McCully
0830-1130	**How a patient-focused approach bridges the gap between the toxicology lab and clinicians (W 101)**	Langevin
	Analytical performance goals for laboratory tests (W 102)	Cartier
1000-1030	Refreshment Break	Confederation Foyer
1000-1500	The Great CSCC Golf Game	Fox Meadow
1130-1330	Lunch on your own	
1230-1330	EPOCC	Steeves
	CACB Training Program Accreditation Committee	Robert Dickie
	Pediatric Focus Group	Campbell
1330-1630	**Reporting of protein patterns and associated clinical conditions in the absence of M proteins from serum protein electrophoretograms: Evidence-based or not? (W 201)**	Langevin
1330-1500	**Reference intervals and biological variation: Theory and practice (W 202)**	Cartier
1500-1630	**The life cycle of a lab test: How to implement change well (W 203)**	Cartier
1500-1530	Refreshment Break	Confederation Foyer
1500-1700	Blood, Sweat and Tears CSCC Charity Walk/Run 2014	
1700-1800	"New Member Network" Reception	Tupper
1800-1900	Opening Ceremonies: **Adding Value to Laboratory Medicine**	Palmer
1900-2130	Opening Reception	Confederation Centre

Monday June 9		
0730-1700	Registration	Confederation Lobby
0730-0900	**IW 001 – Siemens Canada** – Vitamin D Standardization is Now a Reality	Tilley
	IW 002 – Bio-Rad – Introduction of the Risk Calculator Software	Langevin
	IW 003 – Thermofisher – Advances in Ultra-High Resolution Mass Spectrometry and its Application to Clinical Research and Forensic Toxicology	Cartier
	IW 004 – Abbott – Optimizing Quality Control Using Six Sigma Metrics and Technopath Controls	Campbell
0900-1200	**Symposium 1: Appropriate Laboratory Utilization: Navigating back from the d***ark side of the moon*	Palmer
1000-1045	Refreshment Break	Confederation Foyer
1200-1400	Lunch	Pope
1230-1400	**IW 005 – Roche** – Cystatin C is a Useful Tool for Estimating GFR and the Risk of Mortality	Tilley
	IW 006 – Alere – Evaluation of the epoc® Blood Gas System at Royal University Hospital in Saskatoon SK	Langevin
	IW 007 – Technidata – The Role of Biobanks in the Future of Clinical Laboratories	Cartier
	IW 008 – Inter Medico – Automation in Autoimmunity – We are finally catching up!	Campbell
1400-1700	**Symposium 2: Recent Advances in Molecular Diagnostics**	Palmer
1500-1530	Refreshment Break	Confederation Foyer
1700-1900	**Grand Opening of Exhibits -** Exhibitor Wine and Cheese	Confederation
1700-1800	Posters staffed	Confederation

Program Overview

Tuesday June 10		
0730-1700	Registration	Confederation Lobby
1000-1730	Exhibit Hall Open	Confederation
0730-0830	**Breakfast Roundtables (RT 101 – RT109)**	Pope
0730-0900	CSCC Editorial Board	Tilley
0900-1200	**Symposium 3: Advances in Pediatric and Chronic Care**	Palmer
100-1045	Refreshment Break in Exhibit Hall	Confederation
1200-1300	Lunch with Exhibitors	Confederation
1300-1400	**Guided Poster Review**	Confederation
1400-1500	Toxicology Interest Group	Campbell
	Fluids Interest Group	Cartier
	Working Group on Quality Management	Langevin
1400-1600	CALIPER	Tilley
1500-1530	Refreshment Break in Exhibit Hall	Confederation
1500-1600	Monoclonal Gammopathy Interest Group	Campbell
	Autoverification Interest Group	Cartier
	Point of Care Testing Interest Group	Langevin
1600-1730	**IW 009** – **Abbott** – Use of High-Sensitivity Troponin-I for ACS, Analytical Performance and Clinical Performance of the Abbott ARCHITECT hs tn	Tilley
	IW 010 – **Beckman Coulter** – Clinical and Analytical Needs in Vitamin D Assays: and How to meet those Needs	Cartier
	IW 011 – **The Binding Site** - Freelite and Hevylite: Complementary Assays for Better Management of Patients with Multiple Myeloma or other Monoclonal Gammopathies	Langevin
	IW 012 – **Somagen** - Fecal Calportectin: Usefulness in the diagnostic routine approach	Campbell
1730-	Free evening	

Wednesday June 11		
0730-1700	Registration	Confederation Lobby
1000-1300	Exhibit Hall Open	Confederation
0730-0830	CACB Credentials Committee	McCully
0730-0830	**Breakfast Roundtables (RW 101 – RW 109)**	Pope
0900-1200	**Symposium 4: Men's Health**	Palmer
1030-1115	Refreshment Break in Exhibit Hall	Confederation
1045-1115	Meeting of Executive & Exhibitors	Pope
1200-1300	Lunch with Exhibitors	Confederation
1300-1400	**CSCC Annual General Meeting**	Palmer
1400-1500	**CACB Annual General Meeting**	Palmer
1500-1610	Oral presentations	Palmer
1610-1730	**CSCC Town Hall**	Palmer
1830-1930	**President's Reception**	Harbourview Terrace
1930-2400	**Gala Banquet**	Harbourview Ballroom
Thursday June 12		
0800-0900	CSCC Council	Chandler
	CACB Board	J.H. Gray

2014 Joint CSCC-SQBC
Conference Planning Committee

CO-CHAIRS

Dr. Edward Randell Dr. Amy Lou

SYMPOSIA
Dr. Andrew Lyon (Chair)
Dr. Khosrow Adeli
Dr. Edward Randell
Dr. David Kinniburgh
Dr. Edgard Delvin

ABSTRACTS
Dr. Yu Chen (Chair)
Dr. Raymond Lepage
Dr. Peter Kavsak

ROUNDTABLES
Dr. Bassam Nassar (Chair)
Dr. Rasoul Alikhani-Koupaei

WORKSHOPS
Dr. Edgard Delvin

SOCIAL EVENTS
Dr. Amy Lou

LIAISON TO CSCC COUNCIL
Dr. Andrew Lyon
President-Elect

General Information

REGISTRATION
Confederation Foyer, PEI Convention Centre

Saturday June 7	12:00-17:00
Sunday June 8	07:30-17:00
Monday June 9	07:30-17:00
Tuesday June 10	07:30-17:00
Wednesday June 11	07:30-17:00

EXHIBITS
Confederation Ballroom, PEI Convention Centre

Monday June 9	17:00-19:00
Tuesday June 10	10:00-17:30
Wednesday June 11	10:00-13:00

POSTERS
Confederation Ballroom
Monday 17:00-19:00, Tuesday 10:00-17:30 & Wednesday 10:00-13:00

Authors will staff their posters:
Monday 17:00-18:00

SOCIAL EVENTS & MEALS
Tickets for social events will be in the packages of registered delegates and will be collected at each function.

Admission to all sessions and exhibits is by name badge.

YOUR PD CREDITS AT THE CONFERENCE

1. In your registration bag there will be a "Personal Credit Recording Form". This will be your personal record of the codes displayed at each session. The code will be shown on the screen at the symposia about 3 times. As soon as you see it, write it on the form under "Attendance Code". The code will be given verbally by the roundtable and workshop speakers.
2. Enter the claims using the codes, online in the CSCC website.
   - If you are a member, log in and go to "CE Code Entry" under membership tools. Codes for all Category 1 credits can be entered one by one before going to the next step. Category 2 codes must be entered separately.
   - If you are not a member, go to Conferences/Events > Non-Member Certificates, enter the codes, and download a certificate attesting to the credits earned.
3. Industry workshops can be submitted as Category 2 activities.
4. We need your feedback on the sessions offered. This feedback, plus suggestions for future topics is what is used to justify the choice of topics when applying for accreditation in future years. Therefore it is very important that you take a few minutes during each session and complete the evaluation forms.

USING THE APP

To get the CSCC mobile app, follow the instructions below or simply scan* the appropriate QR code below:

- iPhone and iPad users--search "CSCC 2014" on the Apple App Store.
- Android users--search "CSCC 2014" on the Google Play Store.
- Blackberry, Windows, others--go to this address on your smart phones (omit www): https://cscc.gatherdigital.com

iOS **Android** **Mobile Site**

*The device you are scanning with must have a QR code scanner app downloaded

Social Events

SUNDAY JUNE 8, 2014

New Member Network Reception

For current trainees and all Fellows who have graduated within the last four years.
Time: 17:00-18:00
Location: Tupper Room, PEI Convention Centre

Opening Ceremonies

Time: 18:00-19:00
Location: Palmer Ballroom, PEI Convention Centre
Fee: Included in registration fee

Opening Reception

Time: 19:00-21:30
Location: Confederation Centre of the Arts
Fee: Included in registration fee

MONDAY JUNE 9, 2014

Grand Opening of the Exhibits
Exhibitor Wine & Cheese Reception

Time: 17:00-19:00
Location: Confederation Ballroom, PEI Convention Centre
Fee: Included in registration fee

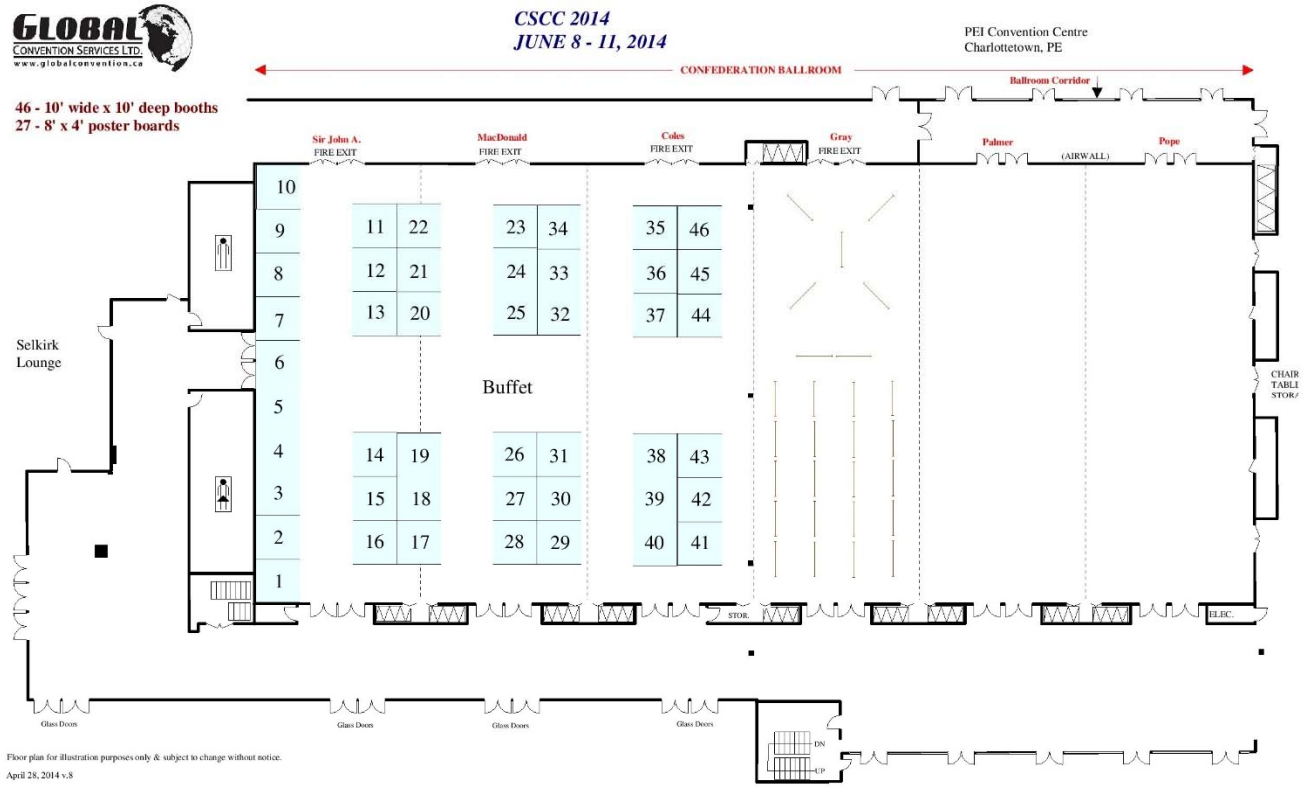
WEDNESDAY JUNE 11, 2014

President's Reception
Gala Banquet

Time: 18:30-19:30 President's Reception
19:30 Banquet
Location: Harbourview Ballroom, PEI Convention Centre
Fee: Included in registration fee; extra tickets - $95/person

Exhibits

Confederation Ballroom
PEI Convention Centre



Booth #	
#38, 39, 40	Abbott Diagnostics
#9	AB Sciex
#2	Alere Canada
#8	Alpco
#1	BD Diagnostics
#32, 33	Beckman Coulter Canada
#36	BioPacific Diagnostic Inc.
#17	Bio-Rad Laboratories (Canada)
#34	CSCC
#16	Cedarlane
#7	Clinical and Laboratory Standards Institute
#27	DBC Diagnostics Biochem Canada
#41, 42	DiaSorin Canada Inc.
#23	Elsevier Science
#15	ESBE Scientific
#37	Hospitals in Common Laboratory

Booth#	
#45	Instrumentation Laboratory
#31	Inter Medico
#14	Nova Biomedical Canada Ltd.
#24, 25	Ortho-Clinical Diagnostics
#30	Qualisys Diagnostics Inc.
#29	Radiometer Canada Ltd.
#18, 19	Roche Diagnostics
#44	Services Technidata Canada Inc.
#3, 4, 5, 6	Siemens Healthcare Diagnostics
#13	Somagen Diagnostics
#26	Sysmex Canada Inc.
#28	The Binding Site Inc.
#20, 21	Thermo Fisher Scientific
#43	VitalSine Inc.
#12	Waters Corporation

Sunday June 8 Afternoon

2 CONCURRENT SCIENTIFIC WORKSHOPS
Refreshment Break in Foyer

W 101 How a Patient-focused Approach Bridges the Gap Between the Toxicology Lab and Clinicians

0830-1130 Langevin Room

Credits: 2.5

Speakers: **When only an unusual specimen type will do**
Dr. Loralie Langman, Dept. of Laboratory Medicine 7 Pathology, Mayo Clinic, Rochester
Breast milk case(s) - Phenobarbital and Primidone, a new metabolic relationship?
Dr. David Colantonio, Pediatric Laboratory Medicine, The Hospital for Sick Children, Toronto
The cocaine-levamisole story; Alcohol availability in the public domain; Tacrolimus – Challenging TDM in a pediatric transplant patient
Dr. Donald LeGatt, Department of Laboratory Medicine, University of Alberta Hospitals, Edmonton

Overview: Toxicology labs frequently get requests from clinicians for the strange and unusual, whether for the detection of novel drugs, for detection/analysis in unusual matrices, or for detection/monitoring of "old" drugs in new situations. These unusual requests can be critical to clinical management of the patient and to understanding the case. This workshop will present examples where discussion between the clinical care team and the laboratory have been critical to understanding the case and providing the care team with meaningful results for the benefit and safety of patients. Needs Assessment Optimal patient care requires collaboration between the clinical service and the laboratory, but this can be a difficult thing to achieve. Case examples of how the gap between the laboratory and clinical care team has been bridged to provide the missing piece of information that was essential for patient management.

Objectives: At the conclusion of this session, participants will be able to explain and apply:
1) Strategies for communicating with clinical care teams
2) Approaches for the analysis of alternate matrices
3) Approaches for detection/analysis of novel drugs and "old" drugs in new situations.

W 102 Analytical Performance Goals for Laboratory Tests

0830-1130 Cartier Room

Credits: 2.5

Speakers: *Dr. Lynn Allen, Laboratory Director, Department of Laboratories, Headwaters Health Care Centre, Orangeville*
Curtis Parvin, Bio-Rad, David Armbruster, Abbott

Overview: Clinical or medical laboratories provide laboratory results and consultation to clinicians to help them in their clinical-decision making and contribute significantly to the quality of patient care. Performance requirements for accuracy and precision should be established in conjunction with clinical input. Evaluation of the performance of assays is required to assure that they meet clinical needs. This evaluation includes:
1) Metrology, which aims at improving the accuracy and comparability of patients' results across different laboratories and different analytical platforms for optimal interpretation of patient results;
2) Laboratory quality control (QC) plans used to monitor the performance of analytical processes and to detect errors;
3) Estimation of measurement uncertainty in the laboratory.

Objectives: At the conclusion of this session, participants will be able to:
1) Identify the steps involved in standardization
2) Understand the steps in establishing traceability of calibrators
3) Understand the challenges and limits in metrology applied to immunoassays.
4) Approach QC design from the perspective of patient risk
5) Assess the impact of QC frequency on the quality of patient results
6) Identify simple and effective QC practices
7) Define measurement uncertainty (MU) and describe its basic components
8) Determine estimates of MU for laboratory tests
9) Describe how MU may be used in assessing the quality of laboratory tests

Sunday June 8 Afternoon

1130-1330	Lunch on your own	
1230-1330	EPOCC meeting	Steeves Room
	CACB Training Program Accreditation Committee	Robert Dickie Room
	Pediatric Focus Group	Campbell Room

CONCURRENT SCIENTIFIC WORKSHOPS
Refreshment Break in Foyer

W 201 Reporting of Protein Patterns and Associated Clinical Conditions in the Absence of M proteins from Serum Protein Electrophoretograms: Evidence-based or not?

1330-1630 Langevin Room

Credits: 2.5

Speakers: *Dr. PC Chan, Clinical Biochemist, Sunnybrook Health Sciences Centre, Assistant Professor, University of Toronto*
Dr. Yu Chen, Division Head, Clinical Biochemistry, Department of Laboratory Medicine, Dr. Everett Chalmers Regional Hospital, Horizon Health Network; Chair, Point-of-Care Testing Committee, Horizon Health Network, Fredericton NB; Assistant Professor, Dalhousie University, Hailfax NS
Dr. Adil Khan, Director, Point-of-Care Testing & Clinical Chemistry, Temple University & Episcopal Hospitals, NACC and TUH-Cancer Center Laboratories; Assistant Professor of Pathology, Temple University School of Medicine, Philadelphia PA (non-presenting)

Overview: Clinical serum protein electrophoresis (SPE) is a well-established technique that separates serum proteins into 5-6 fractions or zones, and serves the primary purpose of detecting and quantifying monoclonal immunoglobulins (M-proteins). However, the reporting of serum protein patterns and their associated (presumptive) clinical conditions, particularly in the absence of a visible M-protein, has been controversial. Based on a recent Canada-wide practice survey sanctioned by the MGIG, the SPE reporting practice was highly variable, despite the availability of consensus guidelines. The authors sought evidence, if any, supporting these practices through literature reviews and laboratory audits.
Three fundamental questions were asked:
1. Does a particular protein pattern reliably predict a clinical/disease condition?
2. Is a particular disease condition related to a monoclonal gammopathy?
3. Does the identification of particular disease condition(s) result in improved detection of monoclonal gammopathies by SPE?

During the workshop, data from various studies will be summarized and critiqued, with a view to addressing the questions above. The audience will also be encouraged to share their rationale or reasons supporting their own SPE reporting practices.

Objectives: At the conclusion of this session, participants will be able to:
1) have a better understanding of the use of serum protein electrophoresis in the investigation of monoclonal gammopathies;
2) be able to appraise the evidence, or a lack of it, in supporting the reporting of protein patterns in the absence of M-proteins, and
3) have improved their skills in rationalizing their practice based on scientific evidence.

W 202 Reference Intervals and Biological Variation: Theory and Practice

1330-1500 Cartier Room

Credits: 1.5

Speakers: *Dr. Khosrow Adeli, The Hospital for Sick Children, Toronto*
Dr. David Colantonio, The Hospital for Sick Children, Toronto
Dr. Dana Bailey, Gamma-Dynacare, Toronto

Overview: Reference values (and reference limits or intervals) provide valuable information to medical practitioners in their interpretation of quantitative laboratory test results, serving as health-associated benchmarks to which individual test

results can be compared. Regulatory bodies governing medical laboratory best practices require that individual laboratories establish or verify reference intervals for all quantitative test methods. According to current guidelines published by the Clinical Laboratory Standards Institute (CLSI), a single reference interval study performed de novo requires the recruitment of at least 120 healthy reference individuals in order to achieve an acceptably high level of statistical confidence—a value based on early studies examining the influence of statistical method usage on the resulting estimate of the normal range. In order to obtain two-sided 90% confidence intervals for the 2.5 or 97.5 percentiles, a minimum sample size of 120 is required. One can easily appreciate the significance of such an undertaking in terms of the time, resources, and associated costs required of laboratories in order to abide by these stipulations for each analyte measured.

This workshop will present both theoretical and practical aspects of establishing reference intervals for clinical laboratory tests for both adult and pediatric populations.
Dr. Adeli will a) present on the theory of reference intervals and CLSI recommendations, b) review the current adult and pediatric reference interval databases available to clinical laboratories, c) discuss the gaps that currently exist in both adult and pediatric populations, and d) highlight current advances and recent initiatives to close the existing knowledge gap.
Dr. Colantonio will give a detailed description of the statistical methods used to establish new reference intervals and validate existing intervals, using specific examples of biochemical markers. Theory and practical use of outlier exclusion, data partitioning, and non-parametric and robust calculation of reference intervals will be discussed.
Dr. Bailey will then present on biological variation as an important factor that must be taken into consideration when interpreting laboratory test results in a clinical setting. Studies of biological variation provide insight into the physiological changes that occur within- and between-subjects for a given analyte. This information is crucial for result interpretation and will be discussed in both adult and pediatric context.

At the conclusion of this session, participants will be able to:
1) Learn the theoretical concepts and practical approaches in establishment of adult and pediatric reference intervals
2) Develop a comprehensive understanding of the statistical methods used in reference interval determination, including outlier exclusion, age- and gender-partitioning, and non-parametric calculation of reference intervals
3) Understand the concept of biological variation, reference value change calculations, and use in establishing analytical goal specifications.

W 203 **The Life Cycle of a Lab Test: How to implement change well**

1500-1630 Cartier Room

Credits 1.5

Speakers: *Dr. Isolde Seiden-Long, Clinical Biochemist, Calgary Laboratory Services, Foothills Medical Centre, Calgary*
Dr. Lawrence de Koning, Clinical Biochemist, Alberta Children's Hospital, Calgary
Dr. Sadrzadeh Hossein, Section Chief, Clinical Biochemistry, Calgary Laboratory Services, Calgary

Overview: Many lab directors start their careers with little or no training to implement changes to testing service. This area has been identified as a gap in the curriculum of Clinical Chemistry and General Pathology training programs. This presentation provides a systematic approach for implementing change that is applicable to all laboratory areas. This workshop describes all the important and necessary steps to implement new tests, introduce changes to tests to the medical staff, and retire tests from clinical service when the time comes. A significant amount of time will be spent on applications of change management to appropriate utilization of laboratory testing, which often involves replacing one test with another, retiring obsolete tests from testing service, or removing tests from panels. Specific examples of successful and unsuccessful changes will be discussed using CKMB and Total CO2 test utilization strategies as examples.

Objectives: At the end of this session, participants will be able to:
1) Describe how the laboratory evaluates requests for new tests and outline a process for delivering a new test to clinicians
2) Describe the requirements for maintaining a test in clinical service
3) List the steps required to retire a test from clinical service
4) Provide specific examples of tests for which utilization has successfully managed, unsuccessfully managed, or replaced / retired from clinical service

Sunday June 8 Evening

1800-1900

Opening Ceremonies

Palmer Ballroom

KEYNOTE ADDRESS:

Adding Value to Laboratory Medicine

Dr. Graham Beastall

President, International Federation of Clinical Chemistry & Laboratory Medicine

Credits: 1.0

Laboratory medicine is at the centre of healthcare. Future developments will reinforce this status. Therefore laboratory medicine specialists have a professional responsibility to deliver continuous quality improvement. In addition, they should seek to add value to improve clinical outcomes and operational efficiency. Two tools will be described and illustrated to help this process. Adding value involves significant activity outside the laboratory and should occur at local, national and international level.

After attending this session, participants will be able to:

1) describe the current and future central role of laboratory medicine in healthcare;
2) understand the concept of 'adding value' and appreciate how they can contribute to this;
3) describe a simple tool to evaluate the value added from innovations in practice..

1900-2130

Opening Reception

Charlottetown Confederation Centre of the Arts

Monday June 9

0730-0900

4 CONCURRENT INDUSTRY WORKSHOPS

Credits: 1.5 (Category 2)

IW 101: Vitamin D Standardization is Now a Reality

Presented by Siemens Canada Limited

Location: Tilley Room

Speaker: *Jim Freeman, Senior Director, Global Assay Development, Siemens Healthcare Diagnostics, Tarrytown, NY, USA*

Standardization programs help with the harmonization of results across manufacturers and methods to improve the diagnosis, treatment, and prevention of diseases. For vitamin D, standardization is necessary to enable the use of established cut-off values for patient categorization and minimize misclassification of patients. For the past several years we have been following the evolution and implementation of the NIH Office of Dietary Supplements Vitamin D Standardization Program (VDSP) and the CDC Vitamin D Certification Program; two complementary programs dedicated to improve the accuracy of vitamin D testing. Now that manufacturers have begun to adopt this standardization and the first results of the CDC Vitamin D Certification Program expect to be available, vitamin D standardization is becoming a reality. This seminar will discuss the VDSP and CDC efforts to date and how laboratories should interpret external proficiency surveys as the VDSP is implemented across the industry.

IW 102 Introduction of the Risk Calculator Software

Presented by Bio-Rad Laboratories

Location: Langevin Room

Speaker: *Curtis Parvin, Manager of Advanced Statistical Research, Bio-Rad Laboratories, Plano, TX, USA*

Laboratories perform quality control (QC) to provide reliable results for appropriate patient care. Data management is an integral part of QC but questions remain. How much QC is necessary? Is there an optimal frequency for running controls? When using a discreet analyzer, what constitutes an assay?
A patient risk approach to QC is a progressive step toward improving quality assurance in patient care.
This presentation will go over the concept of evaluating the risk or reporting an unreliable patient result for your current QC practices and assess realistic alternatives.
We will demonstrate different out of control conditions to determine any potential need for retest.
Using the Risk Calculator software tools, we will generate easy to understand charts to clearly see problem area and explore options to resolve those issues. You will realize that the frequency a lab chooses to run controls and which rules they use to determine acceptable data points play a role. But do you understand how QC rules affect your lab's performance?

IW 103 Advances in Ultra-High Resolution Mass Spectrometry and its Application to Clinical Research and Forensic Toxicology

Presented by Thermo Fisher Scientific

Location: Cartier Room

Speakers: *Marta Kozak, MS, Applications Manager, Thermo Scientific, San Jose, CA, USA*
Dr. Cristiana Stefan, Clinical Biochemist/Toxicologist, Centre for Addiction and Mental Health (CAMH), Toronto, ON

Overview: There is no doubt that, overall, the liquid chromatography (LC) coupled to (tandem) mass spectrometry (MS or MS/MS) has become a reliable and robust analytical technique widely used in the clinical research and forensic toxicology fields. Demands for high bioanalytical needs (such as complex mixtures, low sensitivity, wide range of concentrations, accurate identification), combined with demands for affordable instrument sizes and costs has led to tremendous advances in high resolution mass spectrometry (HR/MS) in recent years. This workshop will describe the general principles of the ultra-high resolution mass spectrometry, and will specifically focus on the ThermoFisher's Q-Orbitrap technology. The importance of mass resolution and exact mass calculation will be taught. Data acquisition experiments along with implementation, advantages and limitations of each experiment in quantitative and screening methods will be discussed. Examples for clinical research and forensic toxicology will be shown. A user's experience will be presented, discussing the acquisition of the Q-ExactiveTM Quadrupole-Orbitrap mass spectrometer in the Clinical Laboratory, and its

evaluation for comprehensive urine drug testing (Centre for Addiction and Mental Health, Toronto, Canada).

IW 104 Optimizing Quality Control Using Six Sigma Metrics and Technopath Controls

Presented by Abbott Laboratories

Location: Campbell Room

Speakers: ***Sten Westgard****, M.S., Director of Client Services, Westgard QC Inc.Orange, CT, USA*
Dr. Jessie Shih*, Ph.D., FACB, Associate Research Fellow, Abbott Laboratories, Abbot Park, IL, USA*

Overview: This workshop reviews the principles of Six Sigma Quality Management with regard to quality control selection. Six Sigma is a well-known quality management approach that uses multiple tools to achieve the goal of reducing errors and defects in a process. As adapted by Westgard to the clinical laboratory, the Six Sigma metric is calculated by combining the traditional measures of analytical quality: TEa (total error allowable), precision, and bias. The choice of quality control materials and QC algorithms is driven by many factors, including the ability of the control material to correctly identify out-of-control situations in method performance (error detection) and to avoid erroneously identifying in-control situations as out-of-control (false rejection). To concentrate on the analytical ability to identify errors correctly and avoid false rejections, laboratories are best served by taking a more quantitative approach to evaluate control performance. Six Sigma provides a useful tool for this purpose. Technopath Multichem controls were evaluated at 4 clinical laboratories and their performance was compared to the lab's current control solution. Six Sigma metrics were calculated for both sets of controls for twelve clinical chemistry assays and twelve immunoassays. Overall performance was comparable between the Technopath Multichem controls and the lab's QC solution. This workshop demonstrates how Six Sigma metrics can be used to evaluate the performance of the Technopath Multichem controls for clinical chemistry tests and immunoassays.

Monday June 9

0900-1200 S1: SYMPOSIUM 1

Location: Palmer Ballroom

Credits: 2.5

APPROPRIATE LABORATORY UTILIZATION: NAVIGATING BACK FROM *The Dark Side of the Moon*

Chair: *Dr. David Kinniburgh, Director, Alberta Centre for Toxicology, University of Calgary, Calgary AB*

0900-0930 *The Transition from Comfortably Numb to High Hopes*. **Why laboratory utilization is under a national spotlight**

Speaker: *Dr. Sherry L. Perkins, Head of Biochemistry, The Ottawa Hospital and Eastern Ontario Regional Laboratory Association, Ottawa ON*

Overview: This session will focus on the historical and current factors which influence laboratory utilization across acute, community and chronic health care programs. The presentation will include a discussion and examples of the financial and quality impacts of laboratory utilization and an introduction and overview of strategies to assess and modify laboratory utilization.

Objectives: At the end of this session, participants will be able to:
1) Understand the factors which influence laboratory utilization
2) Describe the financial and patient care impact of appropriate and inappropriate laboratory utilization
3) Describe high-level strategies and approaches to modify laboratory utilization practices.

0930-1000 *Another Brick in the Wall*: **Building a data-driven approach to test utilization**

Speaker: *Dr. Christopher McCudden, Clinical Biochemist, The Ottawa Hospital, Ottawa ON*

Overview: In order to accurately assess laboratory test utilization, it is necessary to have robust data. A thorough analysis of a robust dataset can challenge assumptions, leverage action, and provide an unbiased view of processes and practices. This session will describe data sources, information management, and data validation in the context of laboratory test utilization. There will be examples of the benefits and challenges of laboratory information systems and administrative health databases and an overview of how they are designed. The session will also illustrate how exploratory data analysis can be used to validate data and inform strategies for change management ranging from a single analyte analysis to region-wide guidelines.

Objectives: At the conclusion of this session, participants will be able to:
1) List sources of data for assessing test utilization
2) Describe challenges and benefits of LIS and administrative health databases
3) Describe strategies for approaching test utilization analysis.

1000-1045 Refreshment Break in Foyer

1045-1115 *Welcome to the Machine*: **How automated analysis and reporting facilitates investigation and monitoring of test utilization**

Speaker: *Dr. Matthew P.A. Henderson, Clinical Biochemist, The Eastern Ontario Regional Laboratory Association, Ottawa ON*

Overview: Understanding lab test utilization often requires highly customized data exploration and analysis. Data analysis should not be the rate-limiting step in identification of aberrant test use. Therefore, once a pattern of data analysis becomes evident it is advantageous to automate the process. This lecture will walk through an approach to automated analysis of test utilization that summarizes test use by ordering physician, location, and patient. Along the way, the programming tools used to automate analysis and reporting will be described.

Objectives: At the end of this session, participants will be able to:
1) Understand an approach to analysis of lab test utilization
2) Appreciate the benefit of customized automated test utilization reports
3) Identify a set of open-source tools for automated data analysis and reporting.

Monday June 9

1115-1145 *Not The Final Cut:* **Building local, provincial and national inter-disciplinary strategic approaches to effective laboratory utilization**

Speaker: *Dr. David W. Kinniburgh, Director, Alberta Centre for Toxicology, University of Calgary, Calgary AB*

Overview: Appropriate utilization is an issue that has captured the attention of many organizations and groups, locally, provincially, nationally and internationally. This presentation will provide an overview of these groups and programs and their activities, highlighting the information and resources available to help individuals develop effective strategies of their own.

Objectives: At the end of this session, participants will be able to:
1) Identify the organizations and programs working on laboratory utilization
2) Identify the resources to help develop their own laboratory utilization strategies.

1145-1200 **Panel Discussion and Q & A**

1200-1400 Lunch in Pope Ballroom

1230-1400 **4 CONCURRENT INDUSTRY WORKSHOPS**

Credits: 1.5 (Category 2)

IW 005: **Cystatin C is a Useful Tool for Estimating GFR and the Risk of Mortality**

Presented by Roche Diagnostics

Location: Tilley Room

Speaker: *Dr. Philip A. Marsden, Professor of Medicine and Division Director of Nephrology, University of Toronto/St. Michael's Hospital, Toronto, ON*

Overview: Current estimates suggest that as many as 1 in 6 people in North America have chronic kidney disease. Knowing which person with chronic kidney disease is at risk to develop end-stage kidney disease or death could tell us who needs intensive monitoring and/ or intervention. The glomerular filtration rate (GFR), the classic measure of kidney function, describes the amount of plasma that is cleared of an endogenous or exogenous marker filtered by the glomeruli per unit time. Until recently, estimating methods were based on serum creatinine as a marker of kidney function. However, because creatinine is also affected by diet, muscle mass or breakdown and tubular secretion, it is not ideal, and a variety of estimating equations have been used. Importantly, cystatin C is particularly useful for estimating kidney function when creatinine production is variable or unpredictable. Two key advances have improved understanding of cystatin C as a kidney disease biomarker. First, international laboratory reference standards for cystatin now exist, important, when multiple laboratories run the test. Second, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) has developed accurate GFR estimating equations, specifically the 2012 CKD-EPI cystatin C equation and the 2012 CKD-EPI creatinine– cystatin C equation, advances over the 2009 CKD-EPI creatinine equation, which itself is more precise than the MDRD Study equation, especially at higher GFRs. Why does the technique for determining eGFR matter? Recent evidence shows that cystatin-C-based eGFR offers improvements in prognosticating mortality and ESRD across diverse populations. This talk will review these general concepts and present this new data.

Monday June 9

IW 006 **Evaluation of the epoc® Blood Gas System at Royal University Hospital in Saskatoon, SK**

Presented by Alere Canada

Location: Langevin Room

Speaker: *Dr. Martha Lyon, Ph.D, DABCC, FACB, Clinical Biochemist (Critical Care & Point of Care Testing), Saskatoon Health Region, Royal University Hospital, Saskatoon, SK*

Overview: This talk will summarize the results of an analytical assessment of the epoc® Blood Gas System relative to the Radiometer ABL800 Blood Gas Analyzer and, where appropriate, the Roche Cobas 6000 Clinical Chemistry Analyzer. Precision of the EPOC system was assessed using 3 levels of Eurotrol quality control material (n=10/QC level). Bias (inaccuracy) relative to the Radiometer ABL800 or the Roche Cobas 6000 was assessed using patient correlation data (N=55) and analyzed with a Passing Bablok regression to determine the line of best fit and its associated slope and intercept values. Total error associated with the measurement of the EPOC analytes was determined taking imprecision and inaccuracy into consideration.
The following formula was used to calculate total error:
Total Error (%) = |%bias| + 1.65*%imprecision
Total error was estimated across the normal and pathological ranges for each of the analytes examined.

IW 007 **The Role of Biobanks in the Future of Clinical Laboratories**

Presented by Services Technidata Canada Inc.

Location: Cartier Room

Speaker: *Yves Charron, MT, Director of Sales, Technidata, Montreal, QC*

Overview: This lecture will describe the role of biobanking in clinical and anatomic pathology laboratories and its relation to personalized medicine and translational research. We will present Technidata's approach to the complex requirement to add value to left over samples and how they can help ensure additional revenue for organizations. We will also approach the roles of laboratory professionals in personalized medicine.

IW 008 **Automation in Autoimmunity - We are finally catching up!**

Presented by Inter Medico

Location: Campbell Room

Speaker: *Dr. Ronald A. Booth, Ph.D., FCACB, Clinical Biochemist, Assistant Professor, The Ottawa Hospital, University of Ottawa, Ottawa, ON*

Overview: Traditionally, the immunology/autoimmune laboratory has been manual, batch oriented and laborious and has not reached the level of automation the other areas of laboratory medicine enjoy. Recently there have been a number of advances in automation including automated slide processing and interpretation. This lecture will discuss the advances in immunology/autoimmune automation and explore the experiences of a large academic hospital laboratory in its transformation from purely manual batch processing to a fully integrated and largely random-access automated state.

Monday June 9

1400-1700 S2: SYMPOSIUM 2

Location: Palmer Ballroom

Credits: 2.5

RECENT ADVANCES IN MOLECULAR DIAGNOSTICS

Chair: *Dr. Edgard Delvin, Montreal Quebec*

1400-1430 Circulating mRNAs as Biomarkers for the Diagnosis of Human Disease

Speaker: *Dr. Vincent De Guire, Biochemist, Clinical Biochemistry Laboratory, Maisonneuve-Rosemont Hospital, Montreal*

Overview: A family of new players has emerged in the last decades in the diagnostic field. Over one thousand miRNAs have been identified in human so far. Hundreds of these small RNAs have been detected in the different biological fluids and biopsies used in our clinical laboratories. At the center of every biological process, they are specifically expressed in human diseases. Perfect for differentiating pathologies of similar etiologies many groups have demonstrated their tremendous potential in a wide range of clinical context. The basics of circulating miRNAs and analytical aspects will be covered and specific applications in renal graft and macular degeneration will be discussed.

Objectives: At the conclusion of this session, participants will be able to:
1) Summarize the basics of circulating miRNAs.
2) List different clinical applications of miRNA profiling in body fluids.
3) Discuss the particularities and challenges of miRNA detection in body fluids.

1430-1500 MicroRNA's in Human Disease

Speaker: *Dr. Victor Tron, Professor and Head, Department of Pathology, Queen's University, Kingston ON*

Overview: This lecture will describe the role of microRNAs in biological regulation in human health. Particular attention will be paid to their role in cancer.

Objectives: At the conclusion of this session, participants will be able to:
1) Understand the role of microRNA in human disease
2) Appreciate the emerging role for microRNAs in laboratory diagnosis

1500-1530 Refreshment Break in Foyer

1530-1600 NGS of cell DNA in maternal circulation to screen for fetal aneuploidy

Speaker: *Dr. Glenn E. Palomaki, Associate Director, Division of Medical Screening & Special Testing, Department of Pathology and Laboratory Medicine, Women & Infants Hospital and Alpert School of Medicine at Brown University, Windham Maine*

Overview: Maternal circulation contains fragments of cell free DNA from both the mother and the fetus. Using next generation sequencing technology, it is possible to screen for a wide variety of fetal disorders from Down syndrome to deletion/duplication syndromes to assembling whole fetal genomes. This rapidly emerging technology is already being integrated into routine prenatal testing protocols.

Objectives: At the conclusion of this session, participants will be able to:
1) Understand how circulating cell free DNA can be sequenced to identify Down syndrome
2) Appreciate the current professional recommendations for use
3) Appreciate the strength and limitations to its clinical use

Monday June 9

1600-1630 Genetics of therapeutic drug response

Speaker: *Dr. Gwendolyn A. McMillin, Associate Professor/Medical Director, University of Utah/ARUP Laboratories, Park City Utah*

Overview: The association of genetic variants with drug metabolism and response has provided opportunity to improve drug selection and optimize dosing for an individual patient. There are many well-characterized associations between genotypes and both pharmacokinetic and pharmacodynamic effects. The U.S. Food and Drug Administration has incorporated information about pharmacogenomics biomarkers into more than 100 drug labels (*http://www.fda.gov/drugs/*), and the Clinical Pharmacogenomics Implementation Consortium is publishing guidelines to support implementation of specific gene-drug pairs (*http://www.pharmgkb.org/page/cpic*). This presentation will highlight successful gene-drug pairs and describe how a genotype can be used to guide pharmacotherapy decisions today. Challenges and barriers to implementation, as well as promising future approaches to pharmacogenetics will also be discussed.

Objectives: At the end of this session, participants will be able to:

1) Describe an example of how pharmacokinetics can be altered by pharmacogenetics
2) Describe an example of how pharmacodynamics can be altered by pharmacogenetics
3) Discuss challenges and barriers that have impeded clinical implementation of pharmacogenetics.

1630-1645 Q & A

1700-1900

GRAND OPENING OF EXHIBITS
Wine & Cheese Reception
Confederation Ballroom

POSTER VIEWING
Authors will staff their posters from 1700-1800

Tuesday June 10

0730-0830

9 BREAKFAST ROUNDTABLES
Breakfast for roundtable participants begins at 0700

Location: Pope Ballroom

Credits: 1.0

RT 101 Testing for testosterone deficiency: Can the lab finally get it right?

Speaker: *Dr. Paul Yip, Department of Laboratory Medicine & Pathology, University Health Network, Toronto*

Overview: Everyone and everywhere are weighing-in on testosterone deficiency. It's the reason behind various campaigns to alleviate aging males of ailments ranging from fatigue and diminished libido, all the way to erectile dysfunction and andropause. While these health concerns are taken seriously, much controversy exists around the diagnosis of hypogonadism and the role of testosterone testing. Several major societies have put forward a variety of guidelines, yet there is no universally accepted threshold of serum total testosterone (TT) that defines hypogonadism. Clearly more studies with meaningful outcomes are needed, but first, the TT measurements need to be standardized and accurate. Recent progress has been made to define rigorously the quality specifications and methodological traceability in support of TT assays that are in routine use. Additionally, the use of bioavailable testosterone (BAT) testing will continue to have utility, while analog-based measurement of free testosterone should no longer be used. With a reliable TT assay in hand, the availability of BAT testing, and an approach to investigation of testosterone deficiency, your laboratory will be able to assist physicians when seeking advice on how to order and interpret testosterone results.

Objectives: At the conclusion of this session, participants will have
1) Explain the pre-analytical variables which affect testosterone measurement;
2) Describe the current state of the art for serum testosterone measurement;
3) Devise an approach for the laboratory investigation of male testosterone deficiency.

RT 102 The interference of contrast agents on laboratory tests

Speaker: *Dr. Yu Chen, Division Head, Clinical Biochemistry, Dr. Everett Chalmers Regional Hospital, Horizon Health Network, Fredericton*

Overview: CT and MRI contrast agents have been demonstrated potential interference on a few laboratory tests, such as clotting time, calcium, phosphate, iron, magnesium, zinc, and urine specific gravity, etc. IVD manufactures developed new NM-BAPTA colorimetric assay for calcium. The contrast agents' impact on this new assay will also be reviewed. * Needs Assessment To avoid potential laboratory test interference, the Contrast Media Safety Committee of the European Society of Urogenital Radiology recommends to not perform non-emergency biochemical analysis including calcium measurement of blood and urine collected within 24 hours of contrast medium injection [(1)]. A complicated algorithm for minimizing a false-positive calcium value has also been developed recently with the consideration of the following factors, the GBCA species, the calcium assays, whether the patients are under acute care or not [(2)]. However, these approaches are not easy resolution for clinical and laboratory practice. We studied on the potential interference of contrasts on the new NM-BAPTA colorimetric assay for calcium and found this new assay is essentially free of MRI contrast interference and is ideal for routine practice [(3)].

[1]. Morcos SK, Thomsen HS, Exley CM; Members of Contrast Media Safety Committee of European Society of Urogenital Radiology (ESUR). Contrast media: interactions with other drugs and clinical tests. Eur Radiol. 2005;15:1463-8.
[2]. Emerson J, Kost G. Spurious hypocalcemia after Omniscan- or OptiMARK-enhanced magnetic resonance imaging. Arch Pathol Lab Med. 2004;128:1151-6.
[3]. Yan R, Tarr H, McNally M, Cartier L-J, Chen Y. 2014. Interference of gadolinium-based contrast reagents on colorimetric calcium assays. Clin Biochem (accepted as is).

Objectives: At the end of this session, participants are expected to:
1) understand the potential interference of contrast agents on laboratory tests.
2) understand the strategies for avoiding contrast agent interference.
3) understand the new development of colorimetric calcium assay without significant contrast agent interference.

Tuesday June 10

RT 103 Free Cortisol: Clinical value and approaches to measurement in urine, saliva and serum

Speaker: *Dr. Morris Pudek, Division of Clinical Chemistry, Vancouver General Hospital, Vancouver*

Overview: Laboratories have traditionally provided measurements of total serum cortisol by immunoassay. Hospital patients, especially those in the ICU may have abnormal levels of binding proteins such as cortisol binding globulin and albumin. As with thyroid hormones it is the free level which is bioactive. We usually assume that approximately 10% of the total cortisol is free and bioactive. However this is often not the case. The percent free cortisol varies considerably with total cortisol level, the binding protein concentration and the presence of competing binding factors. Salivary cortisol and urine cortisol concentrations as measured by immunoassay or mass spectrometry have been used to estimate the free cortisol concentration because the binding proteins have been excluded from these filtrates. I will describe alternate approaches to measure free cortisol in serum using ultrafiltration devices and the advantages and disadvantages of these approaches. In an ICU setting rapid turnaround times for this assay may be required to provide appropriate therapy when adrenal insufficiency is suspected. A simple and practical method will be necessary.

Objectives: At the conclusion of this session, participants will be able to:

1) Understand the clinical role for measurement of free cortisol levels in ICU patients, in patients with suspected adrenal insufficiency, and in suspected Cushing's syndrome.
2) Compare different analytical approaches to the measurement of free cortisol in serum, urine and saliva.
3) Decide which approach would be most practical for your laboratory

RT 104 Trace Elements in Nutrition and Toxicity

Speaker: *Dr. Liju Yang, Clinical Chemistry/Immunology, LHSC, Victoria Hospital, London*

Overview: Trace elements are a group of minerals that are present in the body in trace amounts (ppb or ppt). According to their biological effects, trace elements can be divided into two groups, essential and toxic elements. Essential trace elements, also called micronutrients, are required in small amounts for body's health and normal functions. Deficiency can lead to metabolic disorders. Toxic elements, commonly called "heavy metals", have no nutritional values in human. Even small amounts can interrupt functions of many organ systems, particularly the nervous system.
This roundtable will talk about some common essential and toxic elements, including the sources/route of exposure, health effects, and symptoms of deficiency and toxicity. It will also talk about the most appropriate samples for trace element analysis and interpretation of the test results. Finally, it will talk briefly about the analytical method, high resolution ICP-MS, focusing on the principle and advantages.

Objectives: At the conclusion of this session, participants will be able to

1) Know common essential trace elements and heavy metals and their biochemical effects on our health.
2) Understand how laboratory tests can help diagnose trace element deficiency and heavy metal poisoning.
3) Know which tests to order for a specific element.
4) Know the advantages of ICP-MS for trace element analysis

RT 105 Nonalcoholic Fatty Liver Disease: A silent foe

Speaker: *Dr. Edgard Delvin, Clinical Chemistry, Montreal*

Overview: The rapidly increasing prevalence of childhood obesity has become a major public health concern in developed and developing countries. Hence it is fairly safe to anticipate in next decades a major increase of young adults with the stigmata of the metabolic syndrome (MetS), and of the related non-alcoholic fatty liver disease (NAFLD), that may lead to non-alcoholic steatohepatitis (NASH). Although the majority of individuals with NAFLD do not progress to NASH, those who do are at far higher risk of progression to cirrhosis with subsequent hepatic cell carcinoma. NAFLD is insidious and may go unnoticed for years and its formal diagnosis be incidental when a liver biopsy is requested for other purposes. Under those circumstances, it becomes important to develop robust methods for screening and early diagnosis of these 2 entities. The session will review the pathophysiology, the epidemiology of Nonalcoholic Fatty Liver Disease, and explore the present and upcoming biomarkers.

Objectives: At the conclusion of this session, participants will be able to

1) Describe the epidemiology and the natural history of NAFLD in children and adolescents;
2) Identify current biomarkers for pediatric NAFLD and describe their clinical efficiency;
3) Identify new potential biomarkers for pediatric NAFLD.

Tuesday June 10

RT 106 How well are we measuring and reporting ammonia?

Speaker: *Dr. Isolde Seiden-Long, Clinical Biochemistry, Calgary Laboratory Services, Foothills Medical Centre, Calgary*

Overview: In adults , ammonia levels can be elevated during liver failure or impairment, urinary tract infection, gastrointestinal bacterial overgrowth, due to various medications e.g. valproic acid, chemotherapy, and in-patients on total parenteral nutrition. In babies and children, blood ammonia levels can be increased in inherited defects of the urea cycle, organic acidurias , disorders of fatty acid oxidation, other illness in babies e.g. sepsis, asphyxia, Reye's syndrome and transient hyperammonaemia of the newborn. Due to the underlying clinical causes of ammonia elevation in these populations, the clinical lab often receives lipemic or icteric samples for ammonia measurements. In our own facility, our lab receives approximately 25% of our specimens for ammonia testing either icteric, lipemic or hemolyzed. The analytical requirement for an ammonia method is that it must be relatively robust to these endogenous interferents to reliably report test results. In addition, ammonia is an unstable analyte fraught with preanalytical collection issues which confound clinical interpretation. Recently, our lab has adapted a third party reagent for ammonia to use on our main chemistry platform, as the method we were previously using resulted in dilution or inability to report 20-25% of our clinical specimens. During our evaluation, several issues arose about ammonia testing including preanalytical issues and the technical considerations for conducting inter-site comparisons, a lack of recent reference interval studies for pediatric specimens, and availability of external quality assurance programs measuring ammonia at physiologically relevant levels and providing adequate assessment for measurement accuracy.

Objectives: At the conclusion of this session, participants will be able to
1) Describe preanalytical considerations in ammonia testing
2) Be aware of the currently available methods for ammonia testing and how they compare in terms of their relative performance
3) List available external quality assurance programs and the efficacy of assessment they offer
4) Be familiar with the available reference intervals and critical values used for ammonia testing

RT 107 Shaping the Future of Laboratory Medicine: Your Vision

Speaker: *Dr. Graham Beastall, President, International Federation of Clinical Chemistry & Laboratory Medicine (IFCC), Glasgow UK*

Overview: The delivery of healthcare is undergoing rapid change in all countries in the world. Mega-trends include:
- Advances in understanding the causes and treatment of disease
- Technological advance
- Demographics leading to an increase in chronic disease
- Patient focussed and personalised medicine
- Evidence based medicine
- Flexible healthcare delivery models.
- Balancing increased demand with the need for greater cost effectiveness

These trends all provide opportunities for laboratory medicine specialists. However, realisation of those opportunities requires positive action, often outside the laboratory. The IFCC mnemonic 'SCIENCE' is a convenient tool to help laboratory medicine specialists consider how value may be added to a quality service at local or national level in the interests of better patient care. Roundtable participants will be encouraged to share their thoughts on the future of laboratory medicine as it applies to the service they provide.

Reference: Beastall GH. Adding value to laboratory medicine: a professional responsibility. Clin Chem Lab Med 2013; 51: 221-228

Objectives: At the conclusion of this session, participants will be able to
1) Recognise the global influences on the future of healthcare and the implications for laboratory medicine
2) Understand the ways in which laboratory medicine specialists can 'add value' to improve the quality of service offered to patients
3) Commit to audit the service provided by your laboratory as the first step in formulating a vision for the future

Tuesday June 10

RT 108 HbA1c: Non-technical aspects

Speaker: *Dr. Raymond Lepage, Scientific Director, Biron-Laboratoire medical, Brossard*

Overview: Over the last 20 years, clinical chemists have been mostly concerned with methodological aspects of HbA1c measurement including types of tests and associated interferences, and more recently calibration issues and the use of Hba1c for the diagnosis of diabetes. A review of the literature indicates that many other factors can interfere with the interpretation and signification of Hba1c levels. In this roundtable, participants will discuss these other aspects of HbA1c physiology including the effect of age, sex, race and the notion of fast and slow glycators. Examples from hemodialyzed patients will be used to discuss the impact of factors modifying the half-life of red cells and some of the avenues to cope with this non-technical source of variation. A final discussion will be held on the impact of hypoglycemic episodes on the relation between Hba1c level and diabetes complications.

Objectives: At the conclusion of this session, participants will be able to
1) Understand the impact of non-technical sources of variation affecting %Hba1c levels
2) Discuss equations for adjusting Hba1c levels in hemodialysis patients
3) Know the limitations of the relationship between Hba1c and diabetes complications

RT 109 Comprehensive urine drug testing in the addiction and mental health setting: challenges and solutions

Speaker: *Dr. Cristiana Stefan, Centre for Addiction and Mental Health, Clinical Laboratory and Diagnostic Services, Toronto*

Overview: At the Centre for Addiction and Mental Health (CAMH) in Toronto, the comprehensive urine drug testing (screening and/or confirmation) plays a major role in the clients' initial assessment, management decisions and continuous monitoring. Believe it or not, urine drug testing in the addiction and mental health setting is an on-going challenge. First, the analytical requirements in this setting are more subtle than in the emergency one, although there is a large overlap in the drugs of interest. Second, the questions to answer are more diverse (often results are denied), and to answer them with the highest accuracy it is important that the testing methodology is sensitive, and identifies not only the parent drug but also its metabolites, and preferably more than one metabolite to best support a positive result. The gold standard GC-MS technology has at least two major limitations: extensive and expensive specimen preparation prior to analysis and lack of suitability for glucuronide metabolites, which often are more abundant than other types of metabolites. Lack of commercially available standards further complicates the glucuronide identification. But, what about switching to the LC-HR (high resolution)/MS technology? Could this technology overcome all these limitations and even become the new gold standard for urine drug testing? This session will discuss both challenges and solutions to the complex task of comprehensive urine drug testing in the addiction and mental health setting.

Objectives: At the conclusion of this session, participants will be able to:
1) Learn the specifics of comprehensive urine drug screening in the addiction and mental health setting
2) Discuss the challenges of laboratory testing in the face of result denial
3) Appreciate the role of powerful techniques such as LC-HR (high resolution)/MS to comprehensive urine drug screening in the addiction and mental health setting

Tuesday June 10

0900-1200 S3: SYMPOSIUM 3

Credits: 2.5

Location: Palmer Ballroom

ADVANCES IN PEDIATRIC CRITICAL AND CHRONIC CARE

Chair: *Dr. Khosrow Adeli, The Hospital for Sick Children, Toronto ON*

0900-0930 Recent Advances in Newborn Screening

Speaker: *Dr. Michael Geraghty, Professor, Pediatrics, Children's Hospital of Eastern Ontario, Ottawa ON*

Overview: This lecture will provide an overview of newborn screening in Ontario. The recent addition of Severe Combined Immune Deficiencies (SCID) to the testing menu using molecular techniques will be discussed. Additionally the utility and future applications of molecular biology in newborn screening will be addressed. Finally the lecture will summarise the current debate on the use of pulse oximetry (a point of care test) to screen for Critical Congenital Heart Disease.

Objectives: At the end of this session, participants will be able to:
1) Gain a better knowledge of the disorders screened for in the newborn period and the variety of technologies used;
2) Appreciate the utility and potential uses of molecular techniques in newborn screening;
3) Understand the rationale of screening for Critical Congenital heart disease and appreciate the different challenges inherent in universal point of care testing.

0930-1000 The ICU is Testing ... but what is the question?

Speaker: *Dr. Christopher S. Parshuram, Senior Scientist & Critical Care Physician, The Hospital for Sick Children, University of Toronto, Toronto ON*

Overview: Determination of normal and abnormal ranges in critical illness is challenging. The concept of acceptable is discussed, the importance of the clinical context, and the relevance of understanding the sample described. Several clinical examples are provided that illustrate the importance of lab-ICU communication.

Objectives: At the conclusion of this session, participants will be able to:
1) better recognize the clinical context of critical illness and the nature of critical care units
2) appreciate potential advantages of evaluating clinical monitoring
3) better understand why differences in normal or acceptable may vary.

1000-1045 Refreshment Break in Exhibit Hall

1045-1115 Beyond BMI: New approaches to childhood obesity and chronic disease prevention

Speaker: *Dr. Tracey Bridger, Pediatric Endocrinologist, Associate Professor, Eastern Health, Memorial University, St. John's NL*

Overview: What factors have the biggest influence on health? A lot of attention is focused on weight and lifestyle behaviours, with strong messages about changes needed to become healthier. It is often unrecognized that one's lifestyle behaviours and health are influenced by so many things, including genetics, biology, education, environment, and many other broader factors. There has been so much attention given to childhood obesity and the possible risk associated with it that people tend to focus on weight alone without regards to what is important for health in general.

This lecture will review current evidence on what influences the health of children and what risk factors of later chronic disease start in childhood. We will explore ways to approach and manage these risk factors successfully, without causing harm to the child and family.

Objectives: At the conclusion of this session, participants will be able to:
1) Understand what risk factors (including insulin resistance, inactivity, obesity) of later chroinc disease start in childhood;
2) Appreciate the large role genetics plays in determining our metabolic health;
3) Understand an approach to managing these risk factors successfully, without doing harm

Tuesday June 10

1115-1145 Canadian Health Measures Survey - Addressing Data Gaps

Speaker: *Dr. David Blais, Laboratory Manager, Health Statistics Division, Statistics Canada, Ottawa ON*

Overview: This presentation will give an overview of the Canadian Health Measures Survey (CHMS) and the data available to researchers to generate national statistics. A particular example will be presented on the joint collaboration between the CALIPER program (Canadian Laboratory Initiative in Pediatric Reference Intervals) and the CHMS to establish a healthy reference values for laboratory tests in the Canadian pediatric and adult population. It was identified that major gaps currently exists for laboratory reference values in Canadians and the CHMS data can be used to address these critical gaps. The establishment of these reference ranges will directly contribute to improved diagnosis and care of Canadians.

Objectives: At the conclusion of this session, participants will be able to:
1) Understand how to access CHMS data;
2) Understand how to access CHMS biobank samples;
3) Understand how the Canadian Health Measures Survey can fill gaps on Canadian health statistics

1145-1200 Q & A

1200-1300 Lunch in Exhibit Hall

1300-1400 GUIDED POSTER REVIEW

Moderator: *Dr. Raymond Lepage, Scientific Director, Biron-Laboratoire médical*

Credits: 1.0

1400-1500	Toxicology Interest Group	Campbell Room
	Fluids Interest Group	Cartier Room
	Working Group on Quality Management	Langevin Room
1400-1600	CALIPER	Tilley Room
1500-1530	Refreshment Break in Exhibit Hall	
1500-1600	Monoclonal Gammopathy Interest Group	Campbell Room
	Autoverification Interest Group	Cartier Room
	Point of Care Testing Interest Group	Langevin Room

1600-1730 4 CONCURRENT INDUSTRY WORKSHOPS

Credits: 1.5 (Category 2)

IW 009 Use of High-Sensitivity Troponin-I for ACS, Analytical Performance and Clinical Performance of the Abbott ARCHITECT hs tn

Presented by Abbott Laboratories

Location: Tilley Room

Speaker: *Dr. Peter E. Hickman MBBS, PhD, FRCPA, FFSc, Director of Chemical Pathology, Associate Professor, ANU Medical School, Australia*
Dr. Andrea Lavoie, Cardiologist, Regina Cardiology Associates, Regina, SK
Dr. Anoop Shah, MBChB (Hons), Clinical Lecturer in Cardiology, University of Edinburgh, UK

Overview: This workshop will discuss the change in mindset of the definition of sensitive troponin assays, the use of high sensitivity troponin I for ACS, analytical performance and clinical performance of the newly licensed Abbott ARCHITECT hs_tnI. Research that addresses the future use and utility of hs_tnI will be discussed, as well as recent findings on the use and implications of sex-specific cutoffs and the impact of shortened rule-out times of suspected MI in the ED setting. The users perspective will be discussed, as well as the broader healthcare implications of using a more sensitive assay with sex-specific cutoffs.

Tuesday June 10

IW 010: Clinical and Analytical Needs in Vitamin D Assays: and How to meet those Needs

Presented by Beckman Coulter Canada

Location: Cartier Room

Speaker: *Dr. Jack J. Zakowski, Ph.D., FACB, Director, Scientific and Professional Relations, Beckman Coulter Inc., Brea, CA, USA*

Overview: This workshop will describe current clinical and analytical factors as they pertain to Vitamin D assay performance. Assay format, standardization and traceability, cross reactivity, and biological variation all contribute to the quality of the reported result. Several current Vitamin D methods will be discussed and compared.

IW 011: Freelite and Hevylite: Complementary Assays for Better Management of Patients with Multiple Myeloma or other Monoclonal Gammopathies

Presented by The Binding Site

Location: Langevin Room

Speaker: *Dr. Frank Courjal, Ph.D., Director of Scientific Affairs, The Binding Site, San Diego, CA, USA*

Overview: Accurate measurement of monoclonal proteins in patients with Multiple Myeloma allows clinicians to diagnose and identify responses and relapses as well as helps guide therapeutic decisions. Recent studies by Mayo Clinic, Rochester have identified limitations of standard electrophoretic techniques which may mask patient responses and limit the utility of monoclonal protein measurements.
Despite their limitations, standard monoclonal immunoglobulin measurements are widely used as reference standards. A valuable addition to the quantification armamentarium was the incorporation of serum free light chain measurements in the early 2000's. International myeloma working group guidelines recommend the assay for monitoring oligosecretory and light chain MM patients' responses but also in the majority of Monoclonal Gammopathies. Increasingly, we understand that protein expression profiles of MM patients can change. With clonal heterogeneity and clonal Darwinism being the focus of intense research in the field of MM, the need of additional accurate tools to monitor these monoclonal proteins and their clonal evolution becomes obvious. Serum Heavy/Light Chain assay in complement to serum Free Light Chain assay in a simple protein algorithm may identify intact immunoglobulin, free light chain and non-secretory escapes in addition to bring a higher level of sensitivity, a higher level of simplicity in interpretation and a higher throughput by full automation.

IW 012: Fecal Calportectin: Usefulness in the Diagnostic Routine Approach

Presented by Somagen Diagnostics

Location: Campbell Room

Speaker: *Dr. Wolfgang Papisch, Ph.D., Scientific Advisor, Autoimmunity Diagnostics Division, (IDD), International, Thermo Fisher Scientific*

Calprotectin is a major part of the cytoplasm of neutrophil granulocytes, monocytes and epithelial cells. In inflammation, the leukocytes migrate through the intestinal wall and are destroyed resulting in increased calprotectin levels in the stool. The levels of fecal calprotectin assist in assessing the risk of an inflammatory bowel disease (IBD), e.g. Crohn's Disease (CrD) or Ulcerative Colitis (UC) and allow to differentiate from non-inflammatory conditions such as irritable bowel syndrome (IBS). Contrary to general inflammation markers like CRP or ESR calprotectin is strongly associated to inflammation in the gastrointestinal tract. While IBD are rare diseases, IBS have a high prevalence of between 10% and 20% in the general adult population depending on the diagnostic criteria used. Prevalence of IBS is lower in children, but still significant. Detection of calprotectin levels is a valuable diagnostic tool, in particular in risk assessment and for deciding for/against colonoscopy. As more inflammation – meaning more disease activity – also means more calprotectin released, data indicate that a follow-up disease activity is possible. Recently, fecal calprotectin detection has been adopted by guidelines (e.g. NICE), respectively is in discussion to be implemented, indicating the value of the marker in the diagnostic setup. The amounts of testing carried out have increased significantly in the last years. In modern laboratories full automation of tests is key for efficiency and thus there has been high demand to have a fully automated calprotectin testing available in the routine setup.

Vendor Evening

Wednesday June 11

0730-0830 **9 BREAKFAST ROUNDTABLES**
Breakfast for roundtable participants begins at 07:00

Location: Pope Ballroom

Credits: 1.0

RW 101 **Intra Laboratory Instrument Comparison: Percent difference to Dizzy Score**

Speaker: *Dr. Andrew Don-Wauchope, Hamilton Regional Laboratory Medicine Program, Juravinski Hospital & Cancer Centre (Core Lab Section), Hamilton Health Sciences, Hamilton*

Overview: Background The requirement to monitor between instrument performance is an important part of hospital system that is aiming to provide equivalent results across the laboratory program. There are no routinely used methods for doing this. In 2011 a poster at the CLMC described a means of doing this from our laboratory using percent difference. This procedure has been adapted and improved.

Description of Roundtable The roundtable will describe the theoretical reasons for comparing instruments; provide a worked example of the data used to determine the change from percent difference to DIfference in Z-score for an analYte (Dizzy Score); demonstrate how the Dizzy score has been implemented in Biorad Unity; and provide examples of how this has been useful in QC review. The material described is in the experimental phase in our laboratory system. There is no proven benefit yet. However, it offers a step towards a more robust and standardised monitoring system of instruments within a laboratory group. There will be time for discussion and debate of the merits and disadvantages of the approach chosen.

Objectives: At the conclusion of this session, participants will be able to:
1) compare analytes between instruments;
2) understand the normalization of data;
3) know how to add the Dizzy Score to their QC review.

RW 102 **Implementation of HIL index reflex rules based on the evaluation of the interference of hemoglobin, bilirubin and lipids on automation chemistry analytes**

Speaker: *Dr. Amy Lou, Department of Pathology and Laboratory Medicine, Capital Health, Halifax*

Overview: Analytical interference by hemoglobin, bilirubin and lipids on chemistry laboratory results is a major concern, which may cause incorrect interpretation, wrong diagnosis and inappropriate patient treatment. Sample hemolytic, icteric and lipemic (HIL) index can be determined and reported with most commercially available automated analyzers. Evaluation of the impacts of different levels of HIL on each chemistry assay provides the basis for establishing the HIL reflex rules. Based on the evaluation data, we are able to classify the extent of the interferences for each analyte into minor interference (<10%), medium interference (10-20%) and large interference (>20%) by degrees of HIL index. For example, if the interference for an analyte was < 10% by 4+ hemolysis, the hemolysis checking is not ordered by the middleware. If the hemolysis interference was 10 - 20% then the result is reported with a comment describing the possible interference and “interpret with caution”. If the hemolysis interference was > 20% the results are not reported and a comment is added requesting repeat blood collection. Middleware rules based on the results of the percentage of HIL interference help automated specimen handling and accurate result interpretation.

Objectives: At the conclusion of this session, participants will be able to:
1) Evaluate analytical interference of hemoglobin, bilirubin and lipids on automation chemistry assays
2) Classify the extents of the interferences for each analyte into minor interference (<10%), medium interference (10-20%) and large interference (>20%) by degrees of HIL index
3) Establish HIL index reflex rules in middleware or lab information system for automated specimen handling and accurate result interpretation.

Wednesday June 11

RW 103 Biochemical Differentiation of the Porphyrias

Speaker: *Dr. Matthew P.A. Henderson, Pathology and Laboratory Medicine, The Ottawa Hospital, Ottawa*

Overview: The porphyrias are a group of metabolic disorders that result from partial deficiencies of enzymes required for heme biosynthesis. The biochemical investigation of porphyrias has a long history and is a good example of the value of biochemical analysis in genetic disease. Periodically biochemists are required to assist in test selection for investigation of suspected porphyrias and interpret the results of porphyria testing. This can sometimes pose a challenge because:

1) The diseases are not named after the affected enzyme.
2) Porphyrin precursors have multiple isomers.
3) There are multiple specimen types required: urine, feces, plasma, whole blood.
4) Secondary causes of abnormal porphyrin metabolism are more common than the porphyrias.
5) There is clinical overlap with non-specific symptoms.

This round table will attempt to provide a systematic approach to biochemical differentiation of the porphyrias with the heme biosynthetic pathway as our guide.

Objectives: At the end of this Round Table discussion, participants will be able to:
1) connect the pathophysiology of porphyrias with the clinical presentation.
2) guide test selection in suspected acute and cutaneous porphyrias.
3) interpret biochemical findings in suspected porphyrias

RW 104 High-sensitivity Cardiac Troponin – should we be using sex-specific cutoffs?

Speaker: *Dr. Peter Kavsak, Core Lab, Juravinski Hospital and Cancer Centre, Hamilton*

Overview: It is evident that the newer high-sensitivity cardiac troponin assays have had a major impact with respect to both clinical care and the clinical laboratory. As of 2013, there are now two approved high-sensitivity assays available: high-sensitivity cardiac troponin T (Roche Diagnostics) and high-sensitivity cardiac troponin I (Abbott Laboratories). This roundtable will review the background and evidence for using sex-specific cutoffs for high-sensitivity assays and will provide the forum for a healthy debate in this emerging area and how it may impact clinical care. performance we all have been trained to implement but which for some reason have been lost on the lowly FOBT.

Objectives: At the end of this session, participants should be able to:
1) Appreciate that there are sex and age specific differences with respect to cardiac troponin when measured with high-sensitivity assays
2) Realize that there may be different mechanisms for an elevation in cardiac troponin when using high-sensitivity assays
3) Discuss the evidence for and against using sex-specific cutoffs for clinical care

RW 105 Urban legends surrounding AL-amylosis, its diagnosis and investigation

Speaker: *Dr. PC Chan, Biochemistry and Genetics, Department of Clinical Pathology, Sunnybrook Health Sciences Centre, Toronto*

Overview: Amyloidosis is a relatively rare disease characterized by tissue and organ damage due to the deposition of insoluble fibrillar proteins (amyloids). There are some 25 different proteins that give rise to a variety of clinical syndromes associated with amyloidosis, ranging from asymptomatic, localized disease to rapidly fatal systemic forms. While diagnosis relies primarily on tissue-based demonstration of amyloids in-situ, serum biomarkers of amyloidogenic precursors have played an increasingly important role in the diagnosis and monitoring of amyloidosis, particularly the systemic types. Among the latter, immunoglobulin light chain amyloidosis (AL-amyloidosis) is the commonest.
The rarity and heterogeneity of amyloidosis is probably the cause of many urban legends surrounding the disorders. Some examples are quoted below as circulated in the medical/laboratory community: “Anyone with significant proteinuria or heart failure should be investigated for amyloidosis”, “Serum free light chain assay is the assay of choice for the purpose of investigating amyloidosis”, “A negative serum free light chain assay excludes a diagnosis of amyloidosis”, “A positive serum free light chain ratio in the presence of organ dysfunction establishes a diagnosis of AL-amyloidosis”, “A positive urine Bence Jones Protein reflects the extent of kidney damage and predicts future kidney failure”, and so on. This Round Table will focus its discussion on these urban legends and examining the truth, if any, behind them. Target audience includes Clinical Chemists, Hematopathologists and Medical Laboratory Technologists with some knowledge and experience in monoclonal gammopathy investigations

Wednesday June 11

Objectives: At the end of this Round Table discussion, participants will
1) have a better understanding of what amyloidosis are, and the clinical indications for their investigation;
2) better understand the laboratory investigation of AL-amyloidosis
3) be able to demystify some of the "urban legends" surrounding AL-amyloidosis

RW 106 Importance of male diagnostics prior to assisted precreation treatments

Speaker: *Dr. Lynn Massicotte, Nasci Biologie Médicale inc., Longueuil*

Overview: Women are the ones mostly affected by sub-fertility problems. They are the one for which the clock is ticking. Women endure hormonal injections and surgeries and are missing work repeatedly during fertility treatments. On the opposite, male fertility factor investigation is harmless. Consequently, it has to be conducted as deeply as possible in order to take better therapeutic decisions right from the start, to reduce the general impact of sub-fertility problems, to reduce the impact and the risks of assisted procreation on women and the desired child, to reduce psychological effects of sub-fertility in couples, to reduce waste of time, waste of energy and money. Hormonal profiling is widely used because they are offered on most analytical platforms and results are precise. On the other end, scientific literature is clear about the fact that sperm ability to fertilize relies on more than abundant spermatozoa and mobility. Nevertheless, for most laboratories not only outdated technologies are used to investigate sperm numbers and motility but in most laboratories this is straight out where investigation stops. Consequently, semen of unknown fertilizing power is used during treatments. Yet, computer assisted semen analysis (CASA) parameters are related to sperm fertilizing power. The presence of antibodies can interfere with sperm-oocyte interaction. Poor sperm DNA quality and chromosomal abnormalities are reducing chances of natural conception and assisted procreation success. Spermatozoa internal signaling is better understood now and clinical investigations targeting this process is probably the next step toward understanding what is appearing today as idiopathic male infertility.

Objectives: At the conclusion of this session, participants will be able to:
1) Understand side effects of incomplete male factor sub-fertility diagnostic
2) Be aware of most widely used male sub-fertility analyses around the world, their interpretation and their limits.
3) What technologies and what parameters are the most promising of delivering new and useful answers to better guide fertility treatments.

RW 107 The Expanding Role of the Clinical Laboratory in Medical Psychiatry

Speaker: *Dr. Cristiana Stefan, Centre for Addiction and Mental Health, Clinical Laboratory and Diagnostic Services, Toronto*

Overview: Psychiatric (mental) disorders cover a large array of illnesses, including but not limited to mood-, anxiety-, substance-abuse related-, psychotic-, cognitive-, developmental -, and personality disorders. Relatively recent research and/or surveys have shown that psychiatric disorders are far more prevalent than previously believed. At this point there are no diagnostic tests to identify mental disorders, rather a set of symptoms or behaviour that meet DSM-V (American) or ICD-16 (WHO) criteria are used for diagnosis. The role of the clinical laboratory in the psychiatry field has grown in the past decades, in parallel with the reintegration of psychiatry into medicine. Currently, laboratory tests serve mainly to: 1) rule out non-psychiatry disorders presenting with neurological and psychiatric symptoms; 2) identify and monitor the side effects of the psychiatric drugs; 3) patient preparation prior to electroconvulsive therapy (ECT); 4) therapeutic drug monitoring. Multiple secondary causes of mental disorders exist: infectious, endocrine, metabolic, vitamin deficiencies, or toxins. During this session notable examples of secondary causes will be given. Main classes of psychiatric medication include: antidepressants, mood stabilizers, antipsychotics, anxiolytics, and stimulants. Psychiatric medication carries considerable risk for side effects (hematologic, cardiac, hepatic, metabolic) and treatment resistance is common. This session will focus on the side effects of atypical antipsychotics such as clozapine and olanzapine, and the role of therapeutic drug monitoring. Discussions will also include the role of pharmacogenetics in the personalized administration of the psychiatric drugs, thus contributing to increased treatment response and reduced side effects.

Objectives: At the conclusion of this session, participants will be able to:
1) Understand the current definition, diagnostic and treatment of psychiatric disorders
2) Understand medical disorders presenting with psychiatric symptoms and laboratory tests that help identify neurological and psychological symptoms due to non-psychiatric illness
3) Understand the side effects of the psychiatric drugs and laboratory tests to identify them

Wednesday June 11

RW 108 Hemoglobinopathy Screening of Newborns

Speaker: *Dr. Rasoul Alikhani-Koupaei, Division Head, Biochemistry, IWK Health Centre, Core Laboratory, Halifax*

Overview: Sickle cell disease is one of the commonest haemoglobinopathy in Africa, the Middle East and India. In recent years, its incidence has increased dramatically also in Europe and North America because of the high rate of migration of people from endemic areas. Newborn screening (NBS) for hemoglobinopathies facilitates early identification of affected individuals to ensure the prompt institution of comprehensive medical care for affected newborns. When linked to extensive follow-up and education, NBS has been shown to significantly reduce mortality in children with sickle cell disease. Neonatal screening is useful and cost-effective to ensure early diagnosis and appropriate treatment for infants with sickle cell disease or other haemoglobinopathies. During this talk we will present and discuss the two main technologies available for screening and confirmatory testing on hemoglobinopathy , high performance liquid chromatography and capillary electrophoresis, the analytical validation of those technologies and the current practice and algorithm used for Hemoglobinopathy screening of Newborns in Nova Scotia.

Objectives: At the conclusion of this session, participants will be able to:
1) understand the two main technologies available for screening and confirmatory testing on hemoglobinopathy
2) understand the analytical validation of those technologies
3) understand the current practice and algorithm used of Hemoglobinopathy screening of newborns in Nova Scotia.

RW 109 Autoverification in Clinical Chemistry: From Theory to Practice

Speaker: *Dr. Raffick Bowen, Pathology, Stanford University, Palo Alto CA*

Overview: Autoverification refers to the automatic release of test results received from a laboratory instrument without technologist review. This session will demonstrate the benefits of autoverification using real-life examples.
Needs Assesment: Manual review of chemistry test results by laboratory technologists is very labor-intensive and results in long turnaround times. Implementation of computerized autoverification will reduce turnaround times, allow staff to focus their specialized skills on the more complex or severely abnormal test results, and provide consistency of result review across all shifts, at all times, for all specimens. This roundtable will demonstrate the benefits of autoverification and different ways of stopping problematic results using real-life examples.
Intended Audience: This roundtable is intended for pathologists, laboratory directors, clinical chemists, laboratory managers, laboratory supervisors, and technologists.

Objectives: At the conclusion of this session, participants will be able to:
1) describe the process of autoverification;
2) explain considerations for implementing of computerized autoverification in a clinical chemistry laboratory

Wednesday June 11

0900-1200 S4: SYMPOSIUM 4

Credits: 2.5

Location: Palmer Ballroom

MEN'S HEALTH

Chair: *Dr. Eleftherios Diamandis, Hold'em for Life Chair in Prostate Cancer Biomarkers/Division Head of Clinical Biochemistry, Mount Sinai Hospital and University Health Network, Toronto ON*

0900-0930 Meet the rest of the PSA family members

Speaker: *Dr. Eleftherios P. Diamandis, Hold'em for Life Chair in Prostate Cancer Biomarkers/Division Head of Clinical Biochemistry, Mount Sinai Hospital and University Health Network, Toronto ON*

Overview: PSA is the premier prostate cancer biomarker. Recently, all members of the PSA gene family have been delineated. These 15 kallikrein genes are localized on human chromosome 19q13.4. The genomic organization and the biological functions of all PSA family members will be described.

Objectives: At the end of this session, participants will be able to:
1) understand the gene and protein structure of PSA and other family members;
2) appreciate the applicability of PSA and other kallikrein members as biomarkers for various cancers.

0930-1000 Prostate Cancer Screening - "Dead or Alive?"

Speaker: *Dr. Bassel Bachir, Urologist, Murray Koffler Urologic Wellness Centre, Toronto ON*

Overview: This lecture will provide an overview of the history of PSA and its use in various clinical scenarios. PSA screening for prostate cancer detection remains widely utilized across the world despite ongoing controversy regarding the benefit of PSA. This lecture will provide an overview of the past and present recommendations regarding prostate cancer screening, and will explain why this remains a controversial issue despite the completion of randomized controlled trials. This lecture will try to explain which group of men may still benefit from regular screening with PSA.

Objectives: At the end of this session, participants will be able to:
1) understand why PSA screening remains a controversial issue;
2) appreciate which group of men may still benefit from PSA screening;
3) understand the difference clinical scenarios where PSA is beneficial.

1000-1030 Discovery of male infertility biomarkers

Speaker: *Dr. Andrei Drabovich, Post-Doctoral Fellow, Mount Sinai Hospital, Toronto ON*

Overview: Non-invasive methods for differential diagnosis of male infertility present the unmet needs in the urology clinics. In our presentation, we will discuss these needs, describe our biomarker discovery pipeline and present in detail our work on discovery of male infertility biomarkers. As an example, we recently discovered and validated by mass spectrometry-based SRM assays 18 proteins in 119 seminal plasma samples, identified two protein biomarkers, ECM1 and TEX101, and proposed an algorithm for differential diagnosis of azoospermia forms and subtypes. Clinical assays for ECM1 and TEX101 will replace the majority of diagnostic testicular biopsies, improve the prediction of sperm retrieval and increase the reliability of assisted reproduction techniques.

Objectives: At the end of this session participants will be able to:
1) understand the unmet diagnostic needs in the urology clinics;
2) learn about current approaches to biomarker discovery by mass spectrometry;
3) appreciate advantages and limitations of mass spectrometry for protein biomarker analysis in the clinical laboratory.

1030-1115 Refreshment Break in Exhibit Hall

Wednesday June 11

1115-1145 **Testosterone Deficiency and Replacement - Myths and Realities**

Speaker: *Dr. Ethan Grober, Assistant Professor, Department of Surgery, Division of Urology, University of Toronto, Toronto ON*

Overview: This lecture will review the current evidence on testosterone deficiency and replacement with a specific emphasis on cardiovascular risk and prostate health.

Objectives: At the conclusion of this sessions, participants will be able to:
1) Apply a rational approach to the diagnosis and treatment of testosterone deficiency;
2) Appreciate the treatment options available in Canada;
3) Understand the impact of treatment on health outcomes and symptom response.

1145-1200 **Roundtable Discussion, Q & A**

1200-1300 Lunch in Exhibit Hall (Exhibits close at 13:00)

1300-1400 **CSCC Annual General Meeting**

1400-1500 **CACB Annual General Meeting**

Location: Palmer Ballroom

1500-1610 **ORAL PRESENTATIONS**

Chair: *Dr. Peter Kavsak, Core Lab, Juravinski Hospital and Cancer Centre, Hamilton*

Location: Palmer Ballroom

Credits: 1.0

1500-1510 POSTER 549
Transient early increase in thyroglobulin levels post-radioiodine ablation in patients with differentiated thyroid cancer
Ivan Stevic[a], Tom C. Dembinski[a], William D. Leslie[b]
[a]Department of Clinical Biochemistry, University of Manitoba and Diagnostic Services of Manitoba, Winnipeg, Manitoba, Canada
[b]Departments of Medicine and Radiology, University of Manitoba, Winnipeg, Manitoba, Canada

1510-1520 POSTER 514
Newborn screening for hemoglobinopathies using HPLC and capillary electrophoresis: Initial findings from the Quebec Newborn Blood Screening Program.
Anne Choquette, Jean-Guy Girard, Yves Giguère, Marie-Thérèse Berthier,
Quebec Newborn Blood Screening Program, Service de Biochimie, CHU de Quebec, Quebec City.

1520-1530 POSTER 546
Assessment of galectin-3, N-terminal pro-brain natriuretic peptide and inflammatory cytokines in patients with myocardial injury after initiation of adjuvant trastuzumab therapy
Colleen Shortt [a], Sukhbinder Dhesy-Thind [a], Aidan Snider-McNair [a], Som Mukherjee [a], Peter Ellis [a], Gregory Pond [a], Darryl Leong [a], Peter Kavsak[b]
[a] McMaster
[b] Juravinski Hospital & Cancer Centre, Core Lab

1530-1540 POSTER 539
Pediatric reference value distributions for vitamins A and E in healthy community children: Establishment of new age-stratified reference intervals from a CALIPER cohort
Joshua Raizman, Ashley Cohen, Tracy Theodoro-Morrison, Betty Wan, Mankhun Chan, Caitlin Wilkenson, Victoria Bevilaqua, Khosrow Adeli
Clinical Biochemistry, The Hospital for Sick Children, Toronto

Wednesday June 11

1540-1550 POSTER 538

A comprehensive LC/MS assay for biogenic amines in urine

Jan Palaty, LifeLabs Medical Laboratories, Surrey, BC

1550-1600 POSTER 527

Validation and Evaluation of Fecal Calprotectin Assays in Pediatric Inflammatory Bowel Disease

Saranya Kittanakom[a], Md. Sharif Shajib[a,b], Celynne Hinzmann[c], Kristine Garvie[c], Joceline Turner[c], Dan Brooks[c], Sufian Odeh[d], Robert Issenman[b,d], V.Tony Chetty[a,c], Joseph Macri[a,c], Waliul Khan[a,b,c]

[a]Department of Pathology & Molecular Medicine, McMaster University

[b]Farncombe Family Digestive Health Research Institute

[c]Hamilton Regional Laboratory Medicine Program, Hamilton Health Sciences

[d]Division of Pediatric Gastroenterology, McMaster University

1600-1610 POSTER 533

Identification of Salicyclate Interference with Chloride ISE Using a Laboratory Data-Derived Machine Learning Algorithm

Christopher McCudden, The Ottawa Hospital

1610-1730 **CSCC TOWN HALL**

Don't miss this years "CSCC Town Hall" meeting. Topics will include recognition under provincial health professions regulations, what the CACB is doing to prepare for professional designation, initiatives from the EPOCC committee and the proposed IFCC changes to membership. Join the discussion on these important issues affecting Clinical Biochemists and help to determine the direction of your profession.

1830-2400 **PRESIDENT'S RECEPTION**
GALA BANQUET

Location: Harbourview Ballroom

Thursday June 12

0800-0900	CSCC Council	Chandler Room
0800-0900	CACB Board of Directors	J.H. Gray Room

Invited Speakers

Dr. Bassel Bachir

Dr. Bachir is currently a urologist at the Murray Kofller Urologic Wellness center at the Mount Sinai hospital in Toronto, Ontario, where he is completing a two year clinical and research fellowship in male reproductive medicine. Dr. Bachir has previously completed his urology residency at the American University hospital, affiliated with the American University of Beirut, in Beirut, Lebanon. This was followed by a 2 year postdoctoral research fellowship at McGill University in Montreal, Canada, studying the biology and therapy of urothelial carcinoma of the bladder. He has published previously in the field of urologic oncology, and has participated in and presented at several international urology conferences including the annual American Urological Association conference as well as the Canadian Urological Association conference. He has also contributed to 'The Consumers Handbook of Urological Health', a recent publication by the Canadian Urological Association targeting urology patients and their families. His current research interests include prostate inflammation and its relationship to prostate cancer.

Dr. Graham Beastall, CBE PhD FRCPath FRCP(Glas)

Graham Beastall is the current President of the International Federation of Clinical Chemistry and Laboratory Medcine (IFCC). He works for the UK Government Department of Health as a professional advisor in laboratory medicine. In this role he is responsible for curriculum development for the training of future laboratory medicine specialists.

Dr Beastall worked in the UK National Health Service for 35 years, most recently as Consultant Clinical Scientist and Clinical Lead for the large multi-site Department of Clinical Biochemistry in North Glasgow, Scotland.

Dr Beastall has published >175 peer reviewed original articles, mainly in biochemical endocrinology and evidence based laboratory medicine. He has given >70 invited plenary lectures around the world. He is the recipient of several national and international awards.

Dr Beastall has held numerous representative roles at national and international levels. These include being President of the Association for Clinical Biochemistry and Vice President of the medical Royal College of Pathologists in the UK .

Dr. David Blais

Dr. David Blais is currently a Laboratory Manager for the Canadian Health Measures Survey (CHMS) at Statistics Canada. Dr. Blais's work mainly focuses on Canadian's exposure to environmental contaminant and persistent organic pollutants (POPs) which are analysed in CHMS eight reference laboratories. Dr. Blais is involved in analytical procedure development and validation, biological sample collection, shipping and storage conditions, quality control and proficiency testing, as well as data analysis and publication to ensure the robustness of the CHMS data. He acquired experience in biological chemistry and functional proteomics on hepatitis C during his post-doctorate research at the Steacie Institute for Molecular Sciences, National Research Council and in protein expression and human innate immunity during his doctorate studies at the University of Ottawa.

Invited Speakers

Dr. Tracey Bridger

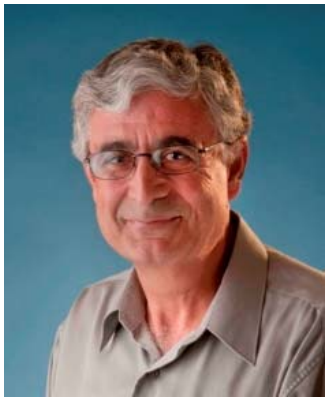
Tracey Bridger is a Pediatric Endocrinologist at the Janeway Child Health Centre and Associate Professor at Memorial University in St. John's, NL. She is co-founder and Medical Director of the Janeway Lifestyle Program and chair of the Healthy Active Living and Sports Medicine Committee of the Canadian Pediatric Society She has done extensive work in the field of healthy active living and chronic disease prevention for children & youth.

Dr. Vincent DeGuire

Dr. Vincent De Guire completed his Ph.D in 2010 in Dr. Gerardo Ferbeyre's laboratory at the University of Montreal. In 2007 he published an article shedding light on the complex regulatory network involving miRNAs and transcription factors in cancer. Selected by the Faculty of 1000 his work has been cited about 400 times. In collaboration with the bioinformatic department, he then developed and validated MultiTar, a program able to generate artificial miRNAs for multitargeting of selected genes. He was recipient of different grants from the Fond de Recherche en Santé du Quebec, the Montreal Center for Experimental Therapeutics in Cancer as well as Grants of Excellence from the Universtity of Montreal.

Completing his post-Ph.D in clinical biochemistry in 2012, Dr De Guire is now part of the team of clinical biochemists and work as biochemist in Maisonneuve-Rosemont Hospital in Montreal. Besides being in charge of specific proteins measurement, automation and samples reception he is also research associate. He is interested in the diagnostic potential of miRNAs more specifically in ophthalmology, renal graft rejection and hematology as well as in development of efficient methods for miRNA detection.

Dr. Eleftherios P. Diamandis, MD, PhD, FRCP(C), FRSC.



Dr. Diamandis is Hold'em for Life Chair in Prostate Cancer Biomarkers, Division Head of Clinical Biochemistry, Mount Sinai Hospital and University Health Network and Professor & Head, Division of Clinical Biochemistry, Department of Laboratory Medicine & Pathobiology, University of Toronto. His research activities evolve around discovery and validation of cancer biomarkers, proteomics, mass spectrometry and translational research.

Dr. Diamandis received his B.Sc. in Chemistry, Ph.D. in Analytical Chemistry and M.D. from the University of Athens, Greece and a Diploma in Clinical Biochemistry from the University of Toronto, Canada. He is a Certified Clinical Chemist by the Canadian Academy of Clinical Biochemistry and the American Board of Clinical Chemistry.

Dr. Diamandis is an active Member of 22 Journal Advisory Scientific and Editorial Boards. He has received numerous awards from both national and international organizations. Dr. Diamandis is also a Corresponding Member of the Academy of Athens, Greece (2005), a Member of the Royal Society of Canada (2008), Fellow of the American Association for the Advancement of Science (2011 and Fellow of the Canadian Academy of Health Sciences (2012). He has published 109 review papers, 540 research papers and co-authored 4 books and 38 book chapters. He is the inventor of 28 issued and 21 pending patents and supervised 20 MSc. and 26 PhD. theses.

Invited Speakers

Dr. Andrei Drabovich

Dr. Drabovich received his PhD in bioanalytical chemistry with Sergey Krylov at York University, Toronto in 2008. After graduation, he started his NSERC post-doctoral fellowship in proteomics at the Lunenfeld-Tanenbaum Research Institute of Mount Sinai Hospital and the University of Toronto with Eleftherios Diamandis. He continued with CIHR fellowship in the same laboratory, focusing on clinical proteomics and translational research. His current research interests include proteomics and mass spectrometry and their application to discover proteins biomarkers of male infertility and prostate cancer, and to identify molecular mechanisms underlying these medical conditions.

Dr. Michael Geraghty

Dr Geraghty is Head of Metabolics and Professor of Pediatrics at Children's Hospital Eastern Ontario and the University of Ottawa. He obtained his medical degree at University College Dublin, Ireland and a MSc in Medical Genetics at Trinity College, Dublin. He completed a Fellowship in Medical Genetics at the Johns Hopkins University School of Hospital and the Howard Hughes Medical Institute from 1988-92. He remained on Faculty there and was Clinical Director of the Institute of Genetic Medicine until 2002.

Dr Geraghty moved to Ottawa in 2002. He was the co- principal in establishing the expanded Ontario Newborn Screening Program in Ottawa in 2006. Currently he is a Medical Consultant to Newborn Screening Ontario. He is Vice Chair of the Newborn and Childhood Screening subcommittee and a member of the Maternal Child Screening Committee in Ontario.

Dr. Matthew Henderson

Dr. Matthew P.A. Henderson is a clinical biochemist at The Ottawa Hospital and an assistant professor in the Department of Pathology and Laboratory Medicine at the University of Ottawa. He is interested in the application of machine learning and large scale data analysis techniques to clinical biochemistry and therapeutic drug monitoring.

Dr. Henderson received his B.Sc. (Hons) in Biochemistry from Queen's University and his Ph.D. in Biochemistry from McMaster University. He completed his post-doctoral fellowship in Clinical Biochemistry at McMaster and is a Fellow of the Canadian Academy of Clinical Biochemistry. He then went on to a second post-doc in the Genetic and Molecular Epidemiology Laboratory at the Population Health Research Institute in Hamilton.

Invited Speakers

Dr. David Kinniburgh, PhD, DABCC, FCACB

Dr. David Kinniburgh is a certified clinical biochemist (American Board of Clinical Chemistry) and a Fellow of the Canadian Academy of Clinical Biochemists and has more than 30 years' experience in clinical biochemistry, toxicology and laboratory management. Dr. Kinniburgh is an Adjunct Professor with the Department of Physiology and Pharmacology, Faculty of Medicine, at the University of Calgary and a Clinical Professor with the Department of Laboratory Medicine and Pathology at the University of Alberta. He is the Director of the Alberta Centre for Toxicology at the University of Calgary and President of the Canadian Society of Clinical Chemists.

Dr. Christopher McCudden

Dr. McCudden is an Assistant Professor in the Department of Pathology and Laboratory Medicine at the University of Ottawa. He serves as a Clinical Biochemist for the Ottawa Hospital and is Laboratory Director for the Glengarry Memorial Hospital and Deep River & District Hospital within the Eastern Ontario Laboratory Association. He is also a Board Member for the National Registry of Certified Chemists.

Dr. Gwendolyn McMillin

Gwendolyn A. McMillin received a PhD in pharmacology, and is certified by the American Board of Clinical Chemistry in both Clinical Chemistry and Toxicological Chemistry. She is currently a Medical Director of Toxicology and Pharmacogenomics at ARUP Laboratories, in Salt Lake City, UT, USA, and an Associate Professor (clinical) of Pathology at the University of Utah School of Medicine. Dr McMillin has been actively involved in professional associations for more than 20 years and recently co-chaired the International Association of Therapeutic Drug Monitoring and Clinical Toxicology's (IATDMCT) 2013 Congress. She also serves as an Editorial Board member for professional journals such as Therapeutic Drug Monitoring and the Journal of Analytical Toxicology, and has published nearly 100 original research manuscripts, review articles, and book chapters. Her research is focused on evaluating and assuring clinical utility of drug testing and pharmacogenomics, funded by several commercial contracts and federal grants.

Invited Speakers

Dr. Glenn E. Palomaki

Dr Palomaki is an Assistant Professor of Pathology and Laboratory Science at Women & Infants Hospital of Rhode Island and the Alpert Medical School at Brown University. He holds undergraduate degrees in Physics (University of New Hampshire) and Computer Science (University of Southern Maine) along with a PhD in Environmental Science and Epidemiology from Queen Mary University of London. Dr. Palomaki's main topics of interest are the evaluation and introduction of screening and diagnostic tests, especially in the areas of genetics. He is a member of the Editorial Board of the Journal of Medical Screening and a member of the College of American Pathologists Resource Committee for Biochemical and Molecular Genetics. Dr Palomaki has authored over 300 articles, chapters and editorials often presents at national and international conferences.

Dr. Sherry L. Perkins

Dr. Sherry L. Perkins is currently the Head of the Division of Biochemistry, Medical/Scientific Director for Pre & Post Analytical Processes and LIS and Co-Director for Point of Care Testing the Ottawa Hospital. She is an Associate Professor in the Departments of Pathology and Laboratory Medicine and Obstetrics and Gynecology at the University of Ottawa.

Dr. Perkins' career path at the University of Ottawa is that of a Clinician Administrator. She has held many leadership roles in Clinical Biochemistry and Pathology and Laboratory Medicine at the local, regional, provincial and national levels. She is a past president of the Ontario Society of Clinical Chemists and of the Canadian Society of Clinical Chemists. She is a member of the Eastern Ontario Regional Laboratory Association (EORLA) Board and Regional Medical Scientific Advisory Committee. In 2013 she was named the inaugural EORLA Regional Biochemistry Discipline Head.

In addition to her experience within the Academic Health Sciences Center of The Ottawa Hospital and University of Ottawa, Dr. Perkins has developed a balanced perspective and understanding of the rural and community environments through her roles as Laboratory Medical/Scientific Director and/or Biochemistry Consultant at various hospitals throughout the Champlain Local Health Integration Network. In addition to her administrative roles and responsibilities, Dr. Perkins has an active research program in partnership with clinical colleagues in the Department of Obstetrics and Gynecology exploring the relationship of biochemical markers to maternal and fetal outcomes.

Dr. Victor A. Tron, MD, FRCPC

Dr. Tron is Professor and Head of the Department of Pathology and Molecular Medicine at Queen's University, in Kingston, Ontario, Canada. Prior to this, Dr. Tron was Professor and Chairman at the University of Alberta. A graduate of the University of Alberta, Dr. Tron completed his specialty training at the University of British Columbia and his Dermatopathology fellowship at the Massachusetts General Hospital. His clinical practice has been limited to Dermatopathology. Dr. Tron has a local clinical practice and has a consultative practice that draws cases from across Canada. His research laboratory is focused on molecular aspects of melanoma. To this end, he has been continuously funded by Canada's national medical sciences granting agency (CIHR) for nearly 20 years. His most recent work has identified a role for microRNAs in melanoma and other skin cancers using both experimental and clinical validation approaches.

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Diurnal Variation of analytes: an underestimated pre-analytical factor in clinical chemistry

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[b]Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Ontario, Canada

Objectives: Diurnal variation is a well known cause of biological variation. We set out to identify analytes affected by diurnal variation, the amplitude of the within day difference and whether collection instructions specified the impact of collection time on test interpretation.

Design and Methods: We identified analytes reported to undergo diurnal variation through a review of Tietz's Textbook of Clinical Chemistry and through a search of Pub Med to capture recent citations. We checked if the time of collection, and its potential impact on test interpretation, was specified in the posted collection procedures issued by two large commercial labs in Ontario.

Results: Our search identified 21 analytes affected by diurnal variation. As expected, cortisol, the archetypal diurnally changing analyte, was the most cited. Hormones represented the major class of identified analytes, but fasting plasma glucose (FPG), MR-proANP, and hepcidin were other noteworthy inclusions. Diurnal amplitude ranged from a low of 1.1 for FPG (still sufficiently large to degrade test performance in ruling diabetes in or out using the cutpoint of 7.0 mM) to a maximum of 65-fold for melatonin. Of the 14 analytes listed in posted collection instructions, the importance of the time of collection was specified for only 5 (36%).

Conclusions: The confounding effect of diurnal variation on test interpretation is underappreciated given that cautions regarding when analytes should be collected were issued in collection instructions only 36% of the time.

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A novel IFNγ-stimulated gene signature is predictive of the survival and chemotherapy responsiveness of breast cancer patients

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[4] Department of Lab Medicine and Pathobiology,
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Background: Breast cancer is a leading cause of death in females. Defects in IFNγ, an essential cytokine in anti-cancer immunity, increase the incidence of mammary tumors. Recently we discovered an IFNγ-stimulated gene signature (ISGS) which is suppressed in cancer cells and potentially participates in the anti-oncogenic effects of IFNγ. Here, we questioned the prognostic value of ISGS in breast cancer patients.

Methods: We performed a bioinformatics analysis to study the correlation between ISGS expression levels and the Overall Survival (OS) or Metastasis Free Survival (MFS) of 8 cohorts of breast cancer patients (GEO database). Patients were sub-classified based on their HER2 and ER status and whether or not they received chemotherapy.

Results: High levels of ISGS strongly correlated with increased OS and MFS in $HER2^+$ ($p = 0.035$) but not $HER2^-$ patients, supporting a selective anticancer role of ISGS. Elevated ISGS was even more protective in $HER2^+;ER^+$ patients ($p=0.004$). ISGS protective effects were seen in untreated patients and the OS was comparable to the OS of chemotherapy treated patients who have low ISGS levels, reconfirming the anticancer role of ISGS. Unfortunately, patients who are both chemotherapy treated and have high levels of ISGS did not survive longer than patients with either elevated levels of ISGS or treated with chemotherapy.

Conclusion: High levels of ISGS correlated with better survival and reduced rates of metastasis in breast cancer patients. Patients with high levels of ISGS are unlikely to benefit from chemotherapy and therefore may be subject to other treatment modalities.

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Comparison of the Abbott ARCHITECT third-generation and Roche Elecsys Anti-HCV Assays in a community healthcare setting

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Objectives: Anti-HCV testing is the first step in diagnosing hepatitis C virus (HCV) infection. Both false-negatives and false-positives are concerning, producing significant diagnostic and psychological consequences, respectively. The objective of this study was to compare the performance of the Abbott ARCHITECT third-generation and the Roche Elecsys Anti-HCV assays in a community healthcare setting.

Design and Methods: 429 serum samples were tested in parallel on both systems; discordant samples were confirmed with the Immunogenetics INNO-LIATM HCV III Score assay.

Results: Concordant results were obtained for 82.1% of samples. Of the discordant samples, 11.1% were positive by INNO-LIA, 68.1% were negative, and 20.8% were indeterminate. For the discordant samples only, the sensitivity and specificity of the ARCHITECT assay were 87.5% and 2.0%; for the Roche assay, they were 62.5% and 95.9%, respectively.

Conclusions: In our patient population, results from the Roche anti-HCV assay more closely correlated with that of the INNO-LIATM HCV III Score assay. The Abbott ARCHITECT Anti-HCV assay appears to have higher sensitivity, but reduced specificity. These findings may be a result of the antigen constructs used: both Roche and INNO-LIA utilize recombinant NS3 synthesized in E. coli in addition to synthetic peptides; Abbott, on the other hand, relies on a recombinant fusion protein (NS3 + core) generated in E. coli and a chimeric fusion protein (human superoxide dismutase + amino acids 1569 -1931) generated in yeast.

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A Direct Comparison of the Ability of Capillary, Agarose Gel and Agarose Gel with Immuno-fixation Electrophoresis to Identify Monoclonal Immunoglobulin Proteins in Human Serum

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Objectives: To compare the respective abilities of a capillary and a gel-based electrophoresis platform to detect the presence of serum monoclonal immunoglobulin proteins.

Design and Methods: 193 samples were analyzed using the Sebia capillary electrophoresis (CE), Sebia Hydrasys 2 agarose gel electrophoresis (GE) and Hydrasys 2 gel immunofixation electrophoresis (IFE) platforms. The ability of the CE and GE systems to detect monoclonal imunoglobulins was evaluated relative to the IFE findings, which was considered to be the definitive method.

Results: The obtained CE and GE results had a 92% concordance rate, with 31% of samples testing positive for a monoclonal protein. Relative to the IFE results, the respective accuracies, sensitivities, specificities and negative predictive values of the CE and GE methods were comparable (95%, 95%, 95%, and 98% versus 96%, 95%, 97%, and 97%, respectively), but the positive predictive values (PPV) differed (89% versus 95%). Both CE and GE had three false negative results, one of which was common to both methodologies. All 11 false positive (FP) results (seven findings for CE and four for

GE) were unique to each protocol; a 17-month follow-up of patients' laboratory results did not identify the development of a monoclonal immunoglobulin in any of these patients.

Conclusion: The overall performance of the CE and GE methods were comparable, however CE suffered from a lower PPV. Long-term follow up of patients with FP results may be warranted to determine the true ability of CE and GE to identify early stage gammopathies.

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Comparison of the Nova StatStrip(R) Lactate versus the Arkray Lactate Pro(R) meters for Fetal Scalp Lactate Measurement

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Objectives: Fetal scalp lactate measured by point-of-care devices has emerged as a useful biochemical marker of fetal acidemia, assisting physicians in deciding whether it is safe to delay delivery or to proceed to immediate delivery. Decision cut-offs for this application as reported in the literature had been determined using the Arkray Lactate Pro. The recent discontinuation in the manufacture of the Lactate Pro prompted us to evaluate the Nova StatStrip Lactate.

Design/Methods: In Phase 1 of the study, evaluation of the StatStrip Lactate and Lactate Pro meters for precision, accuracy and linearity was performed by measuring lactate on venous, arterial, and capillary whole blood specimens on both meters and compared against results on a GEM4000(R) whole blood analyzer. In Phase 2, both meters were compared in a clinical care setting on same fetal scalp samples obtained from women in labour with abnormal fetal heart rate.

Results: In Phase 1, precision of the StatStrip Lactate was excellent, having a 7 %CV at 0.6 mmol/L and 4.9 %CV at 6.4 mmol/L. Comparison with the GEM4000(R) yielded a regression of StatStrip = 0.96*GEM + 0.84, r2 = 0.99, versus Lactate Pro = 0.95*GEM + 0.15, r2 = 0.95. In Phase 2, preliminary data obtained from same fetal scalp samples (n = 67) showed good agreement, StatStrip = 1.03*Lactate Pro + 0.02 and r2 = 0.85.

Conclusion: The StatStrip Lactate demonstrates excellent analytical performance and gives similar values to the Lactate Pro, indicating that clinical decision cut-offs may be adopted from the Lactate Pro.

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Differences in bilirubin and biliverdin interferences in an enzymatic acetaminophen assay.

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Objectives: The interference of bilirubin in enzymatic acetaminophen (paracetamol) measurements has been reported on a number of instrument platforms. Since quantification of acetaminophen levels in overdose is important for patient management, we quantified the false-positive increase in measured acetaminophen in icteric samples. Additionally, both bilirubin (reduced) and biliverdin (oxidized) may be elevated in hepatic failure and so we also quantified the interference of biliverdin.

Design and Methods: Patient samples were collected to generate high and low bilirubin or acetaminophen pools. Exogenous biliverdin was prepared and diluted into the blank patient pool. Serial dilutions of bilirubin, biliverdin, acetaminophen, and combined samples were carried out. Measurement utilized the Abbot Architect platform.

Results: A false acetaminophen level (≥20µmol/L) was generated when total bilirubin measured >140µmol/L (Icteric index 143) with acetaminophen increasing by approximately 75% upon doubling of bilirubin. Exogenous biliverdin generated a similar false acetaminophen level when added to >63µmol/L in the low patient pool. Doubling the biliverdin concentration increased measured acetaminophen by 150%. Dilutions of acetaminophen-containing patient samples spiked with bilirubin and/or biliverdin revealed a similar increased potency of positive interference of biliverdin over bilirubin. In graphical analysis of the acetaminophen assay's increase in absorbance over time for both acetaminophen and biliverdin, the end-point absorbance levels are reached within seconds and remain unchanged for many point readings following. However, bilirubin exhibits a slower rate, suggestive of a slow conversion of bilirubin to a form reactive with the assay.

Conclusions: Both bilirubin and biliverdin are positive interferences of the enzymatic acetaminophen assay.

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Pediatric reference intervals for specialty endocrine and chemistry biomarkers on the Abbott Architect ci4100 System: A CALIPER study of healthy community children

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Clinical Biochemistry, The Hospital for Sick Children

Background: Growth and development can influence circulating biomarker concentrations, hence accurate reference intervals based on healthy pediatric cohorts are essential for assay interpretation. The CALIPER (Canadian Laboratory Initiative on Pediatric Reference Intervals) program, a national research initiative aimed at closing gaps in pediatric reference intervals, is developing a database of covariate-stratified reference intervals for several endocrine and special chemistry markers using the Abbot ARCHITECT ci4100 platform.

Methods: Healthy children and adolescents recruited for the CALIPER study filled out questionnaires including demographic information, and provided blood samples. We measured a number of endocrine and chemistry markers using the Abbott ARCHITECT ci4100 system and reference intervals were established utilizing 367-763 samples per assay. Age- and sex-specific analyte concentrations and variance were visually inspected. Statistically-relevant age/gender-based partitions were determined, outliers removed and reference intervals calculated using CSLI C28-A3 guidelines.

Results: The following analytes showed age-related changes in variance and/or concentration: Beta-2 microglobulin, high-sensitivity CRP, cystatin C, albumin BCG, albumin BCP, pancreatic amylase, SHBG, cholinesterase E, C-peptide, insulin, DHEA-S and ceruloplasmin. Testosterone (2nd GEN) age-related changes were much more pronounced in males. Other analytes measured were Alpha-1 antitrypsin, AGP, Anti-CCP Anti-TPO, glucose, IgE and rheumatoid factor.

Conclusions: The complex expression profiles of several endocrine and chemistry biomarkers were observed, allowing establishment of age- and sex-specific reference intervals. This will enable accurate diagnosis of pediatric patients monitored by the Abbott ARCHITECT ci4100 system in healthcare institutions worldwide. These reference intervals must be validated by each laboratory for the local pediatric population as recommended by CLSI.

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Closing the gaps in pediatric population reference values for cancer biomarkers: A CALIPER study of healthy community children

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Objectives: The CALIPER (Canadian Laboratory Initiative in Pediatric Reference Intervals) program, a national research initiative aimed at closing the gaps in pediatric reference intervals, sought to develop a database of covariate-stratified reference value distributions for 11 key circulating tumor markers including those used in assessment of patients with childhood or adult cancers.

Design and Methods: Healthy community children from birth to 18 years of age were recruited to participate in the CALIPER project with informed parental consent. Participants completed questionnaires and were assessed according to established inclusion and exclusion criteria. Serum samples from approximately 400-700 children were analyzed on the Abbott

Architect ci4100 and reference intervals were established for Alpha-Fetoprotein (AFP), Ant-Thyroglobulin (Anti-Tg), Human Epididymis Protein 4 (HE4), Cancer Antigen 125 (CA125), Cancer Antigen 15-3 (CA15-3), Cancer Antigen 19-9 (CA19-9), Pro Gastrin-Releasing Peptide (ProGRP), Carcinoembryonic Antigen (CEA), Squamous Cell Carcinoma Antigen (SCC), as well as Total and Free Prostate Specific Antigen (PSA) according to CLSI C28-A3 statistical guidelines.

Results: Significant fluctuations of biomarker concentrations by age and/or gender were observed in 10 of 11 biomarkers investigated. Age partitioning was required for CA15-3, CA125, CA19-9, CEA, SCC, ProGRP, Total & Free PSA, HE4 and AFP while gender partitioning was also required for CA125, CA19-9, Total & Free PSA.

Conclusions: The establishment of pediatric reference intervals for tumor biomarkers will not only aid in harnessing the full potential of tumor markers in a pediatric population but also in research aimed at determining the value of tumor marker use in various cancers.

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CLSI-based transference of the CALIPER database of pediatric reference intervals to Beckman Coulter clinical chemistry assays

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Objectives: Accurate pediatric reference intervals obtained in healthy community children are essential for accurate diagnosis of diseases in children. The CALIPER program established a comprehensive database of age- and sex-stratified pediatric reference intervals for over 70 common biochemical markers, which was directly applicable for assays performed on the Abbott ARCHITECT ci4100 system. To ensure a wider application of the CALIPER database, we expanded its scope to Beckman Coulter Synchron DxC800 assays.

Design and methods: First, 200 pediatric pooled patient serum specimens were analyzed on the Abbott ARCHITECT ci4100 and the Beckman Coulter DxC800. Data were subjected to regression analysis, standardized residual, Bland-Altman, and quantile-quantile plots to measure correlation, providing R^2 values. A total of 34 chemistry, lipid/lipoprotein and protein markers were assessed. Next, 100 serum samples from the CALIPER cohort (healthy children) were assayed on the Beckman system and reference intervals were validated using CLSI C28-A3 criteria.

Results: Most (22) of the analytes showed excellent correlation between the Abbott and Beckman systems ($R^2 \geq 0.95$). Ten analytes showed strong correlation (R^2 0.77 ≤ 0.94). Two analytes (carbon dioxide and calcium) showed poor correlation and were not transferable. Most transferred reference intervals determined using the Beckman system were validated through analysis of CALIPER reference samples.

Conclusions: The current study allows successful transference of a large number of chemistry markers from the CALIPER database to assays on the Beckman Coulter DxC800 platform. Validation should facilitate the broad application of CALIPER reference intervals at pediatric centers worldwide, thereby greatly extending their utility.

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Pediatric reference intervals for 29 endocrine and special chemistry biomarkers on the Beckman Coulter DxI Immunoassay System: A CALIPER study of healthy community children

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Background: Accurate reference intervals based on a healthy pediatric population are essential for test result interpretation, since growth and development can influence circulating biomarker concentrations. The CALIPER (Canadian Laboratory Initiative on Pediatric Reference Intervals) program, a national research initiative aimed at closing gaps in pediatric reference intervals, is developing a database of covariate-stratified reference intervals for endocrine and special chemistry markers on the Beckman Coulter DxI Immunoassay System.

Design and methods: Healthy children and adolescents recruited as part of the CALIPER study filled out a questionnaire including demographic information, and provided a blood sample. We measured 29 biomarkers using the Beckman Coulter DxI Immunoassay System utilizing 443-636 samples per assay. Age- and sex-specific analyte concentrations and variance were visually inspected. Statistically relevant age/gender-based partitions were determined, outliers removed and reference intervals calculated using CSLI C28-A3 guidelines.

Results: The following analytes showed age-related changes in variance and/or concentration: AFP, ferritin, prolactin, thyroglobulin, SHBG, vitamin B12, cortisol, DHEAS, folate, free T3, free T4, total T4, insulin and ostase. Estradiol, progesterone, FSH and LH age-related changes were more pronounced in females, and testosterone age-related changes were more pronounced in males.

Conclusions: The complex expression profiles of 29 endocrine and special chemistry biomarkers were observed, allowing calculation of age- and sex-specific reference intervals specific to the Beckman Coulter DxI Immunoassay System. This will enable accurate diagnosis and laboratory assessment of children monitored by this platform in healthcare institutions worldwide. These reference intervals must be validated for the local pediatric population as recommended by CLSI.

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Pseudo hyperbilirubinemia in anicteric blood

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Objectives: The aim of this study was to investigate potential interference on a 65-year-old man's anicteric plasma giving spuriously high bilirubin results on the Roche Cobas 6000.

Design and Methods: Total bilirubin (TBIL) was repeated on the Roche Integra 400 and Modular P, and a dilution (1:4, 1:5, and 1:15) study was conducted. Split specimen aliquots were also measured on analyzers from 4 different manufacturers. Immunoglobulins (Igs) were measured and based on the elevated IgA level; the patient's primary care provider was advised by the Laboratory to bring the patient in for serum and urine protein electrophoresis examinations.

Results: All Roche analyzers generated elevated TBIL although icteric index was 1 (approximately 1 mg/dL or 17 µmol/L level). The dilution study demonstrated non-linear results. Direct bilirubin (DBIL) was measured as normal. TBIL measurements by Abbott, Siemens, Beckman, and Ortho analyzers were all normal. Serum IgG, IgM, and IgA were 3.9, 0.1, and 39.2 g/L respectively. Protein electrophoresis revealed an IgA-λ monoclonal protein (approximated to be 38.3 g/L) and a small peak of lambda free light chains in serum, and prominent lambda free light chains in urine (27.3 g/day).

Conclusions: This rare case is consistent with a few reports in the literature showing that paraprotein may interfere with TBIL assays, especially on Roche analyzers by forming precipitate with the solubilising agent.. This is the first time that an IgA-λ monoclonal protein and possibly lambda free ligh chain involvement have been reported. Being aware of this interference may lead to investigation and possible early diagnosis of multiple myeloma.

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Evaluation of Roche Urisys 2400 system

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[b] Department of Pathology, Dalhousie University, Halifax, Nova Scotia, Canada

Abstracts

Objectives: To determine the performance of the Roche Urisys 2400 system.

Methods: The Roche Urisys 2400 was evaluated on with-in run precision, and total precision. Comparison study was conducted against the Bayer Clinitek 500 analyzer and a refractometer (for specific gravity) on 200 patient urine specimens. The results were considered concordant if they were within 1 grading difference.

Results: The Roche Urisys 2400 system demonstrated an excellent with-in run precision on 3 abnormal urine specimens in that all parameters showed same grade agreement, except that only 1 glucose and 1 bilirubin result out of total 52 had one grade difference. Total imprecision was indicated as good (Table 1). Comparison study demonstrated acceptable concordance on all parameters against the Bayer Clinitek 500 (Table 2). Specific gravity comparison showed Urisys 2400 = 0.9663xRrefractometer + 0.0236, R^2 = 0.994, bias = 0).

Conclusions: The Roche Urisys 2400 system is acceptable for routine urinalysis.

Table 1: Total imprecision of the Roche Urisys 2400 system on the Bio-Rad urinalysis liquicheck (UAL1 and UAL2) quality control samples (expressed as: same grade agreement % / 1 grading difference %, n=20).

	pH	Leukocytes	Nitrite	Protein	Glucose
UAL1	60%/40%	100%/0	100%/0	100%/0	100%/0
UAL2	100%/0	90%/10%	100%/0	100%/0	100%/0
	Ketone	**Urobilinogen**	**Bilirubin**	**Erythrocytes**	**Specific gravity**
UAL1	100%/0	100%/0	100%/0	100%/0	100%/0
UAL2	100%/0	95%/5%	100%/0	100%/0	100%/0

Table 2: Comparison of the Roche Urisys 2400 system with the Bayer Clinitek 500 (expressed as: same grade agreement % / 1 grading difference %, n=200).

pH	Leukocytes	Nitrite	Protein	Glucose
47.5%/43.5%	77.5%/21.5%	100%/0	80.5%/7.5%	98%/2%
Ketone	**Urobilinogen**	**Bilirubin**	**Erythrocytes**	
78.5%/21.5%	94%/3%	98%/2%	73.5%/24.5%	

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Performance evaluation of Roche Integra Homocysteine assay

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Objectives: The aim of this study was to evaluate the new Roche Integra Homocysteine assay (packaged with Diazyme reagent), which is based on a novel enzyme cycling method principle.

Design and Methods: The Roche Integra Homocysteine assay was evaluated on the Roche Integra 800 analyzer using the Clinical and Laboratory Standards Institute evaluation protocols. The method comparison study included the Axis-Shield enzymatic assay (n= 41). In addition, 6 College of American Pathologist (CAP) 2013 proficiency survey samples were used to evaluate assay accuracy against chromatographic method (of 13 laboratories) and enzymatic method (of about 240 laboratories) means.

Results: The Roche Integra Homocysteine assay demonstrated an excellent precision in that with-in run imprecision and total imprecision were 1.3% and 2.3% at 12.6 µmol/L level and 1.1% and 2.1% at 38.3 µmol/L level. There is no obvious carry-over effect. This assay correlated well with the Axis-Shield assay with a slope of 0.9428, intercept of 1.1827, and R^2 =0.9795, average bias of 0.3 µmol/L (4.1%). Roche Integra Homocysteine assay showed good accuracy (-5.7% and -7.2% biases against chromatographic method means and enzymatic method means on the CAP samples).

Conclusions: The Roche Integra Homocysteine assay is an acceptable assay for clinical laboratories.

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Newborn screening for hemoglobinopathies using HPLC and capillary electrophoresis: Initial findings from the Quebec Newborn Blood Screening Program.

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As per the Ministry of health's mandate, newborn screening (NBS) for hemoglobinopathies started on November 4th 2013 in Quebec, initially for the Greater Montreal area. The NBS laboratory is equipped with two high-performance liquid chromatography (HPLC) instruments for 1st tier testing, and abnormal results (2nd tier) are repeated using capillary electrophoresis (CE). To our knowledge, we are the first in America to implement a HPLC-CE design for newborn screening.

Objectives: To illustrate the complementarity of HPLC and CE in the interpretation of results for hemoglobinopathy newborn screening.

Design and Methods: Newborn blood specimens from filter paper dried spots were first analysed with the Biorad VARIANT™ nbs System. Abnormal or indeterminate results were repeated using Sebia Capillarys 2 Neonat Fast.

Results: Analytical correlation between these technologies showed excellent results (n= 56). Three months after implementation, 18621 samples have been tested using HPLC, while 450 samples were retested using CE as 2nd tier. We identified 5 samples (0.03% of all samples, 1.1% of 2nd tier tests) for which initial interpretation by instruments software was not similar and needed further comparison of spectra to identify the appropriate haemoglobin variant.

Conclusions: Despite a good correlation, we observed rare discrepancies in haemoglobin variant calls between both technologies, which have complementary strengths and limitations. Implementation of NBS using both HPLC and CE by the Quebec Newborn Blood Screening Program should help to improve sensitivity and specificity, and thus the overall performance of newborn screening for hemoglobinopathies.

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Test utilization review: Focus on Testosterone

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Objectives: Hospitals and medical centers offer a vast variety of laboratory tests. Clinicians often have insufficient knowledge of the right utilization of tests, resulting in unnecessary or redundant results. The clinical biochemist is the health professional that is most qualified to detect these errors, and promote the correct use. Through identification of the most problematic tests, specific advice and education can result in large-scale economic benefit and optimization of patient care.

Design and Methods: By analysis of ordered tests on the basis of combinations that are often wrongly made, problematic tests can be identified. Additionally, these requests can be linked to a certain department or clinicians, to find the biggest source of incorrect use of laboratory tests.

Results: With data collected over a 1 year period at Maisonneuve-Rosemont Hospital in Montreal, we determined a problematic test: Testosterone (Total, Free, or Bioavailable). Of the 3834 Total Testosterone tests that were ordered we identified 497 (13%) requests of Total Testosterone + Measured Free Testosterone, whose combination does not meet the Endocrine Society recommendations. Of the 245 clinicians that ordered these double requests, 6 were responsible for 20% of the total inappropriate requests.

Conclusions: Analysis of ordered tests allows the identification of inappropriate use of laboratory tests along with the most problematic prescribers, so education and discussion with clinicians can be focused on the most profitable area's, aiming for large-scale economical savings and improved patient care.

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Bupropion exposure in an infant: a case report

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Objectives: Studies show 66 - 80% of nursing women are on medication. While some drugs are safe, there is accumulating evidence of toxicity in some breastfed infants. The objective of this study is to investigate the risk of drug exposure in nursing infants. We present a proof-of-principle case of infant bupropion (BUP) exposure highlighing the importance and clinical applicability of this study.

Methods: We established a drug safety monitoring program, Drugs in Lactation Analysis Consortium (DLAC), to measure several drugs commonly used by women breastfeeding. We worked to create a simplified drug extraction method using organic solvents to facilitate efficient drug extraction from both the lipid and aqueous phases of breast milk. Methods were then developed to measure these drugs using LC-MS/MS.

Results: A 6.5 month old previously healthy infant presented to SickKids Hospital with vomiting and seizures. She was exclusively breastfed; her mother was taking escitalopram daily for several months, with the recent addition of BUP. The usual clinical workup was negative. The infant's urine was tested and was positive for BUP and escitalopram. Serial breast milk and serum samples were obtained and BUP and its major metabolite, hydroxybuproion, were measured using HPLC-MS/MS and BUP levels were determined to be significant around the time of the event. Discharge diagnosis was BUP-induced seizures.

Conclusion: Given the increasing use of medication in nursing women, there is urgency to investigate the potential adverse events associated with infant drug exposure through breast milk and provide guidance for drug use in nursing mothers.

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Evaluation of a method to detect prozone/hook effect/antigen excess phenomenon for Free Light Chain quantification using a simple pooling protocol

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Objectives: Antigen excess is an important issue that can lead to underestimation of patient's results and misdiagnosis. With patient samples which can range from less than 1mg/L to over 100 000mg/L, serum free light chain (FLC) measurement is especially prone to this interference.

Design and Methods: We propose a methodology based on sample pooling for a fast and cost effective method to detect antigen excess phenomenon for serum free light chain quantification. Our strategy was evaluated on the Immage (Beckman) and on the BNII (Siemens) nephelometers using the Freelite® assay (The Binding Site).

Results: First, we evaluated the sensitivity of our strategy using a pool of 15 mixed samples spiked with different concentrations of kappa or lambda free light chain. Secondly, patients with antigen excess ranging from 1192 to 8500 mg/L of kappa free light chain were efficiently detected using our strategy. Finally, a preliminary evaluation of the size of the pools was conducted using pools ranging from 15 to 43 different samples. Based on the precision of the method, our preliminary data suggest that the number of samples in a pool can reach up to 43 different patients to detect an antigen excess of 1192 mg/L.

Conclusion: We described and validated a strategy based on sample pooling for detection of antigen excess on free light chain measurement. This approach could be suitable for any laboratory measuring serum free light chain that does not currently have an instrument platform for detection of antigen excess.

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A Canada-wide practice survey on serum protein electrophoresis: Opportunity for standardization and improvement

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Background: Serum protein electrophoresis (SPE) is a long established technique used primarily for detecting and quantifying monoclonal immunoglobulins or components (MC). However, evidence suggested that substantial variations in reporting practices still exist to date. The objectives of this study are to (1) identify areas and extent of variations in the use and reporting of SPE through a Canada-wide practice survey, and (2) seek possible solutions.

Methods: Under the auspices of the CSCC Monoclonal Gammopathy Interest Group, we devised and conducted a nation-wide survey which consisted of 15 questions each with multiple responses and individual free-text elaborations. The practice survey was open to all CSCC members through a web link to the questionnaire on istant.ly. Participants were instructed not to complete more than one survey from each laboratory.

Results: 43 laboratories participated with 29 completed the whole survey. Some 60% participants used gel electrophoresis while the same % resolved serum proteins into 6 fractions. 66% used SPE as the sole first line test for MC detection, and about one third used SPE also for investigating non-MC conditions. 78% participants would perform reflexive testing if an MC was present but only 47% would do so based on specific protein patterns while the other half would not even comment on findings other than MC.

Conclusions: Substantial variations in test utility and result reporting, especially in the absence of a discrete MC, were present. A lack of good evidence/data surrounding these practices appeared to be the major obstacle for variation reduction.

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Screening and characterization of vitamin D binding protein variants

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Objectives: The gene (GC) for the vitamin D binding protein (DBP) shows a great deal of variation. Two missense mutations (D432E and T436K) are the major common polymorphic variants, and both may influence vitamin D metabolism. However, many other less common variants, identified biochemically, have been reported in literature. This study aimed to identify the underlying mutations by molecular screening and characterize the mutant proteins by mass spectrometry.

Methods: Denaturing high performance liquid chromatography (DHPLC) was used for screening genetic variants on meta-PCR products of the genomic DNA samples. Sanger sequencing identified the specific mutations. A mass spectrometric immunoassay method was used to characterize the DBP protein variants in serum samples.

Results: Molecular screening identified 10 samples (out of 761) containing a recurrent alanine deletion at codon 246 in exon seven (p.Ala246del, c.737_739delCTG) and 1 sample (out of 97) containing a cysteine to phenylalanine substitution at codon 311 in exon eight (c.932G>T, p.Cys311Phe). The mutant allele proteins and posttranslational modified products were distinguishable from the wild-type proteins by mass spectra profiling. Loss of disulfide bond due to loss of cysteine at residue 311 was accompanied by the appearance of a novel mixed disulfide species, consistent with S-cysteinylation of the protein product.

Conclusions: Our results confirm earlier biochemical studies suggesting that some deleterious mutations in the DBP gene are not uncommon. Mutant proteins are secreted and can be found in circulation. By combining molecular screening and mass spectrometric methods, mutant DBP species can be characterized and their potential functional role explored.

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Use of procalcitonin in the acute exacerbation of chronic obstructive pulmonary disease in the emergency room : A costs/benefits and hospital practice short study

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Objectives : Utility of procalcitonin (PCT), a new marker allowing early detection of bacterial infection, in acute exacerbation of COPD (AECOPD) was evaluated in our emergency room (ER). Influence of PCT results on antibiotics prescription and treatment duration, as well as costs/benefits ratio, were addressed.

Design and Methods : PCT analyses were performed stat on a Mini-Vidas (Bio-Mérieux). ER physicians were asked to complete a survey and to rely on an adaptation of a published algorithm. Follow-ups of hospitalized patients were managed by family physicians. PCT data and surveys were analysed.

Results : 33/45 (73%) PCT measurements were adequate. Of those, 29 had a well completed survey. Four hospitalized patients were also included in the study even though not consulting initially at the ER. Procalcitonin results guided decision to prescribe antibiotics (or not) in 70% of the cases. Consequently, 61% of patients (20/33) did not receive antibiotics following a negative PCT result. However, once antibiotics were initiated, subsequent negative PCT measurements had little effect on reduction of treatment duration (11% of hospitalized patients, and 15% upon discharge). The costs/benefits ratio was poor. Savings on antibiotics represented only 18% of costs generated by PCT analyses.

Conclusions : Although not cost-effective in the short term, the use of PCT could lead to significant long term benefits and savings through the reduction of antibiotics prescription, which could ultimately lead to a reduction in cases of *C. difficile* infection and antibiotic's resistance in our community.

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The diagnostic role of B-Type natriuretic peptide in pediatric populations; a systematic review.

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Objectives: B-type natriuretic peptides (BNP) and N-terminal pro-B-type natriuretic peptides (NT-proBNP) have been established as biomarkers of heart failure (HF) in the adult population. However, research evidence on the diagnostic significance of these markers in pediatric and neonatal populations remain limited. This systematic review examines the diagnostic utility of BNP and NT-proBNP in paediatric and neonatal populations with HF, respiratory (RD), and congenital heart diseases (CHD).

Design and Methods: We searched literature published between 1989 and 2013. 332 articles examining pediatric populations were isolated and screened. We included 19 articles using BNP and NT-proBNP as diagnostic tests in urgent-care and non-emergency settings.

Results: Neonatal patients have markedly elevated serum BNP and NT-proBNP levels compared to pediatric populations across all study populations. BNP differentiated cardiovascular-related RD from primary RD (decision range: 100 pg/mL to 550 pg/mL, sensitivity range: 78% - 100%). NT-proBNP was able to differentiate CHD from healthy cohorts (decision range: 2000 – 2850 pg/mL, sensitivity range: 74 – 90%) while BNP diagnosed underlying HF in CHD patients (decision range: 30 – 100 pg/mL, sensitivity range: 62% - 100%). Both BNP (decision range: 31.2 – 313.3 pg/mL, sensitivity range: 83 – 100%) and NT-proBNP (178 – 3617 pg/mL, sensitivity range 81 – 100%) diagnosed HF of various aetiology and severity in pediatric and neonatal populations.

Conclusions: BNP and NT-proBNP may be a useful diagnostic tool in assessing cardiovascular dysfunctions in pediatric patients. Further investigations with BNP in pediatric urgent-care settings are encouraged to more pragmatically evaluate its diagnostic significance.

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Impact of a shortened centrifugation protocol for common chemistry and immunology testing on different automation platforms

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Objectives: There are no standard centrifugation protocols for processing blood specimens in laboratories. Vendors recommend centrifugation at 1000-1300g **Relative Centrifugal Force (**RCF) for 10 minutes. This study evaluates an abbreviated centrifugation protocol at 2600g RCF for 5 minutes.

Design and methods: Two pairs of venous blood samples from four healthy volunteers were collected into serum separator (SST) and plasma separator tubes (PST) (Becton Dickinson). One pair of SST and PST was randomly assigned to our current centrifugation protocol at 1800g for 10 minutes. Another pair was subjected to the abbreviated protocol at 2600g for 5 minutes, 53 analytes including immunology and serology, were analyzed on Architect ci16200, DxC800, Centaur and Immage platforms. The impact of centrifugation protocols on analyte results was determined using paired t-test and average % difference.

Results: There were no significant differences in the results from the two centrifugation protocols (P>0.05), except for ferritin (Architect i2000); P=0.02. The average % differences for all analytes were less than 5%, except for PTH on Architect i2000 and GGT on DxC800 which were -5.98% and -5.33% respectively.

Conclusions: Our results demonstrate that the shorter centrifugation protocol does not adversely affect analytical results for all assays. Faster sample processing will improve turnaround time and efficiency of laboratory operation.

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Is cocaethylene a marker of ethanol use in cocaine users?

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Objective: Cocaethylene (CE) is formed if alcohol is consumed with cocaine. CE is suggested to be a marker of alcohol use in these patients. We wanted to know if CE is indeed a marker of alcohol with cocaine use.

Methods: During the month of April all urine samples that were positive for BE (benzoylecgonine) by CEDIA immunoassay were analyzed for the presence of alcohol and Ethyl Glucuronide (EtG) (both by CEDIA assays) and by GCMS for the presence of cocaine metabolites. Urine creatinine and urine glucose were also measured.

Results: Of the 3122 samples received during the month of April, 160 (5.12%) were positive for BE and were further subjected to GCMS analysis. The GCMS positives results were as follows: cocaine = 39 (24.4%), methylecgonine = 152 (95%); CE = 10 (6.25%); nor-cocaine = 8 (5%); ethyl ecgonine (EE), a metabolite of CE = 18 (18%); and EtG = 83 (51.8%). Correlations BEG and EtG r = 0.2251 p=0.004.

Conclusions: Of the 160 BE positive samples there were 39 that were positive for cocaine suggesting that these patients had used cocaine shortly before voiding. Of these 39 samples 24 were positive for EtG confirming recent alcohol use. Of these 24 samples 10 (41.6%) were positive for CE whereas EE, the metabolite of CE, was positive in 18 (75%) of these 24 samples. Although literature suggests CE as a marker of alcohol use, our results suggests that EE may be a better marker of cocaine and alcohol use.

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Assessing the long-term stability of total bilirubin protected from light under refrigerated conditions

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Objectives: Laboratories often archive samples after biochemistry testing, mainly under refrigerated conditions (2-8^{0}C), and most often for quality assurance testing or medico-legal requirements. Refrigeration aims to stabilize certain analytes; however this does not apply to all analytes, especially analytes that are photolabile, such as bilirubin. In our laboratory after an external quality assurance (EQA) discordant result for total bilirubin (target=32umol/L, original result=26umol/L) we retested the same specimen which was refrigerated for 3.5-weeks and protected from light and produced a result of 19umol/L. Literature is scant on long-term stability (i.e.,>48h) for bilirubin stored in the refrigerator. Accordingly, we investigated stability of total bilirubin as part of our EQA discordant investigation.

Design and Methods: Stability of total bilirubin was assessed by preparing two different patient pools (pooled heparin plasma from 10 patient samples to obtain two pools spanning the EQA sample concentration; i.e., pool-A=31.5umol/L; pool-B =51.7umol/L at baseline). The pools were refrigerated (2-8^{0}C), wrapped in foil, and stored inside a closed cardboard box and were tested (n=10 within-run measurements) every week for a month. A change was considered significant from baseline if any of the mean weekly concentrations exceeded the significant change limit (SCL=mean ±2.8X usual SD; as calculated from Abbott's stated imprecision of 5%).

Results: There were no significant differences in total bilirubin up to 2-weeks; however by the 3rd and 4th -week both pools yielded lower mean results (28.0 and 26.3umol/L; 43.3 and 39.4umol/L, respectively).

Conclusions*:* Total bilirubin protected from light is stable up to 2-weeks when stored at 2-8^{0}C.

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The utility of galectin-3 and high-sensitivity cardiac troponin assays to predict short-term serious outcomes in patients presenting early after chest-pain onset

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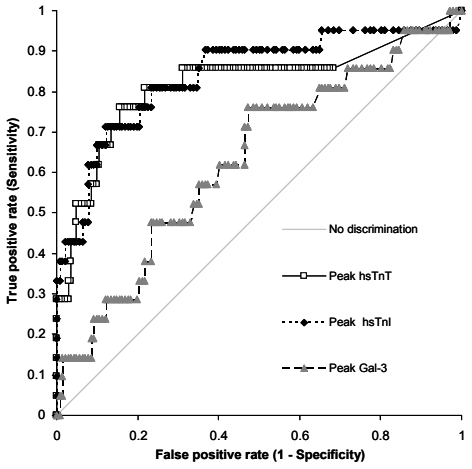
Objectives: In the quest for biomarkers to compliment cardiac troponin (cTn) in the early identification of myocardial injury in patients presenting with chest pain, we assessed the diagnostic performance of galectin-3 and high-sensitivity cardiac troponin (hsTn) in predicting short-term serious cardiovascular events.

Design and Methods: In 163 patients presenting early after chest-pain onset (Clin Chim Acta 2013;419:39-41), we measured 0, 3 and 6-hour levels of galectin-3, hsTnI (Abbott ARCHITECT) and hsTnT (Roche) The outcome was the composite of myocardial infarction, heart failure, serious arrhythmia, refractory ischemic cardiac-pain, or death over the next 72h. We performed non-parametric and receiver operating characteristic (ROC) curve analyses via Analyse-it, Statsdirect, and R software.

Results: There was no difference in the area under the curve (AUC) for hsTnI or hsTnT at 0, 3, and 6h with both assays correlated to galectin-3 at these time points (spearman rho≥0.39; p<0.05). The peak concentration for hsTnI (AUC=0.84) and hsTnT (AUC=0.82) was significantly higher than the peak galectin-3 (AUC=0.63) (p<0.05)(Figure). Combining galectin-3 with either hsTnI or hsTnT did not improve the AUC.

Conclusions*:* Galectin-3 is inferior to hsTn for early-risk prediction and does not appear to provide additional information in setting.



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Comparison of Anti-dsDNA Measurements between BioPlex® 2200 and Farr Radioimmunoassay: Longitudinal Monitoring in Systemic Lupus Erythematosus (SLE)

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Background: The Farr radioimmunoassay is well established in the diagnosis of SLE and monitoring of disease activity. Our study aims to evaluate the ability of Bio-Rad BioPlex multiplex immunoassay to monitor anti-dsDNA antibody levels within individual patients over time in comparison with the Farr RIA.

Methods: Patient results for anti-dsDNA from the Toronto Western Hospital Rheumatology clinic were extracted from August 2010 to October 2013. Agreement between the Farr and BioPlex assays was analyzed from 2088 patients for the most recent result. Trending analysis was performed from a subset of 293 patients with at least 4 serial measurements from both assays collected at the same time. The direction and magnitude of change between paired samples was assessed independently using the reference change value (RCV) and non-parametric Spearman's correlation.

Results: The manufacturer's cut-off limits for positivity were used to interpret anti-dsDNA results as positive or negative. Overall agreement between the Farr and BioPlex assays was moderate (53.4% positive agreement, 92.3% negative agreement, 82.1% overall agreement, Kappa=0.49). The trend analysis based on both RCV and Spearman's rho was considered together with positive and negative interpretation of results. In the subset of 293 patients, 103 showed parallel trends that were observed using either approach. However the overall agreement in the result interpretation among the consistent trends was no different from the remaining results.

Conclusion: Our preliminary study suggests that the BioPlex anti-dsDNA assay provides an alternative to Farr for serial monitoring in certain SLE patients. Further analysis is needed to understand the discordances.

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Validation and Evaluation of Fecal Calprotectin Assays in Pediatric Inflammatory Bowel Disease

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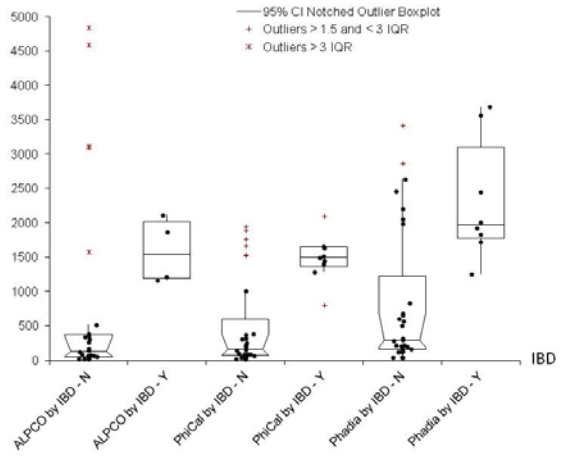
Background: The incidence and prevalence of Inflammatory Bowel Disease (IBD) has increased dramatically in children. Colonoscopic evaluation is necessary in IBD assessment. However, repeated colonoscopy is invasive, expensive, and inconvenient for the patient. Fecal calprotectin (FCal), an abundant neutrophil protein, is proposed as a noninvasive and specific marker of gut inflammation. Our study aimed to validate and analytically evaluate three currently used methods for FCal in stool samples from pediatric IBD patients.

Designs: Stool samples were collected from 40 pediatric patients with confirmed IBD based on clinical and histological criteria. FCal was extracted using a smart-prep extraction kit. The evaluation of linearity, imprecision, and method comparison was performed utilizing PhiCal®Calprotectin-EIA, Phadia250EliACalprotectin, and BÜLHMANN Quantum-Blue Calprotectin point-of-care testing (POCT) and was analyzed via Analyse-it.

Results: Our study demonstrates adequate linearity, imprecision for both immunoassays. A method comparison (IBD-grouped) for the assays is shown (figure). There was no difference in the AUC [AUC of 0.83(PhiCal®), 0.84(Phadia250EliA) and 0.83 (BÜLHMANN)].

Conclusion: The between-assay variation is noted due to the lack of assay standardization and sampling variation. We propose that the FCal test together with the clinical history would be a cost-effective and non-invasive tool to assess pediatric IBD.



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Evaluation of Hemoglobin J-Baltimore Interference on HbA1c Measurement using Capillary Electrophoresis

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Background: Hemoglobin A1c (HbA1c), N-terminus nonenzymatic glycation of b-globin chain, is a biochemical marker of long-term glycemic control and is related to risks for diabetic complications. Hemoglobin (Hb) variants usually interfere with HbA1c measurement, resulting in an overestimated or underestimated value.

Method: Several methods have been used for HbA1c measurement with high-performance liquid chromatography (HPLC) being favored. Recently, capillary electrophoresis (CE) has shown to be a reliable alternative to HPLC. In 2013, Hamilton Regional Laboratory Medicine Program (HRLMP) implemented the Capillarys2 Flex-Piercing,CE,Sebia analyzer for HbA1c routine testing. Interference studies from other Hb variants were included as part of the instrument validation.

Results: The HbJ-Baltimore variant was found to cause a falsely low HbA1c fraction (Prim Care Diabetes 2008;2:155-7). The underestimation of HbA1c in a diabetic HbJ-Baltimore patient was shown using Bio-RadVARIANT™II TURBO (11.1%; Capillarys2Flex-Piercing and 8.9%; Bio-RadVARIANT™II TURBO). In contrast, the result was comparable in a non-diabetic patient who carries the same variant (5.4%; Capillarys2Flex-Piercing and 5.9%; Bio-RadVARIANT™II TURBO). While Capillarys2Flex-Piercing can completely separate the HbJ and HbA peak giving an accurate result for calculating HbA1c, Bio-RadVARIANT™II TURBO does not provide the appropriated resolution to report an accurate HbA1c result.

Conclusion: The short analysis time and high-throughput Capillarys2Flex-Piercing provides a rapid and reliable separation of HbA1c. Calibrators used in Capillarys2Flex-Piercing are IFCC/NGSP certified. No interference with labile HbA1c and major Hb variants; S,C,E,D was found. This observation emphasizes that Hb variants may interfere with the HbA1c assay especially in any diabetic patients and an alternate method should be recommended.

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A randomized, open label, crossover study examining impact of Prograf and Advagraf on mycophenolic acid pharmacokinetics in kidney pancreas transplant patients.

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Objectives: Advagraf is a new modified release preparation of tacrolimus formulated for once daily dosing providing similar exposure to Prograf, a tacrolimus twice-daily dosing formulation. Tacrolimus has been shown to have a variable impact on mycophenolic acid (MPA) pharmacokinetics; however, there is a paucity of data on the impact of Advagraf on MPA pharmacokinetics. We hypothesize that once daily Advagraf can be substituted at the equivalent daily dose for twice daily Prograf in stable kidney pancreas transplant recipients without clinically meaningful changes in MPA pharmacokinetics, tacrolimus exposure, renal allograft function or adverse effects.

Design and Methods: In this prospective crossover study, 8 stable kidney pancreas transplant recipients on twice-daily tacrolimus (Prograf) were randomized to receive Advagraf or Prograf for 12 weeks after which they were crossed over to the other formulation for another 12 weeks. MPA pharmacokinetic profiles were examined using a limited sampling strategy before randomization (baseline), at 12 weeks and 24 weeks. Additionally, patients had their trough tacrolimus levels monitored and their immunologic status was measured using the Cylex ImmuKnow assay at baseline, 12 weeks, and 24 weeks. Patients also completed a self-reported adherence questionnaire at each visit and provided data concerning drug related adverse effects.

Results: Pharmacokinetic analysis revealed that MPA ACU (mean ± SD) was not significantly different at baseline, and following 12 weeks of Advagraf or Prograf were 48.51± 25.97, 49.28 ± 15.24, and 48.63 ± 16.43 mg*h/L, respectively.

Conclusions: We conclude that MPA exposure is not altered when switching patients from Prograf to Advagraf.

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Measurement of serum free cortisol in septic shock patients

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Introduction: It is important to identify septic patients with relative adrenal insufficiency who may benefit from corticosteroid therapy. Free cortisol is the physiologically active form. The proportion of bound cortisol is highly variable and dependent on concentrations of cortisol and binding proteins.

Objectives: To compare methods for free cortisol measurement for identification of adrenal insufficiency in septic shock

Methods: Serum specimens were collected from septic shock patients in the ICU. A protein-free serum was obtained by ultrafiltration using Centrifree Ultrafiltration Devices (Merck Millipore Ltd). Serum free cortisol was then estimated by measuring cortisol in ultrafiltrate. The methods for cortisol measurement include immunoassay (IA) with and without extraction of serum ultrafiltrate, liquid chromatography tandem mass spectrometry (LC-MS/MS), and these results were compared with salivary free cortisol by LC-MS/MS.

Results: This is a pilot clinical study with 10 septic shock patients. Results of serum free cortisol by IA and LC-MS/MS as percentage of serum total cortisol is seen in Table 1.

Table 1. Mean % serum free cortisol by IA and LC-MS/MS

Serum Free Cortisol by IA	28.0 ± 18.2
Serum Free Cortisol by IA after Extraction	22.1 ± 12.5
Serum Free Cortisol by LC-MS/MS	13.8 ± 8.7
Salivary Free Cortisol by LC-MS/MS	13.2 ± 12.4

(n = 10, mean ± SD)

Serum free cortisol by IA without extraction of ultrafiltrate (y) correlates very well with IA following extraction of ultrafiltrate (x) ($y = 0.6838x + 17.572$, $R^2 = 0.9835$) and is comparable with LC-MS/MS method (x) ($y = 0.4242x + 13.667$, $R^2 = 0.9142$). The serum cortisol IA on ADVIA Centaur is precise, CV < 7%. Further study will be done to determine precision of ultrafiltration step and define reference intervals of serum free cortisol by IA without extraction of ultrafiltrate.

Conclusion: Direct measurement of serum cortisol by IA using ultrafiltration is a simple and reliable method to estimate free cortisol for adrenal function assessment in septic shock.

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Evaluation of the IDS-iSYS 1,25 dihydroxy vitamin D immunoassay

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[b] University Health Network, Toronto
[c] Inter Medico

Objectives: To evaluate the analytical performance of the IDS-iSYS 1,25 dihydroxy Vitamin D immunoassay.

Design and Methods: The assay utilizes a monoclonal anti-1,25 dihydroxy vitamin D antibody for immunopurification followed by quantification with a competitive one-site chemiluminescent immunoassay. Precision was evaluated using 2 levels of assay controls (n=19), 2 levels of extraction controls (n=32) and a pooled patient sample (n=31). Linearity was assessed using a pooled patient sample diluted to span the measurement range. Lot-to-lot variation was evaluated using 23 patient samples and two lots of reagent (n=23). Method comparison studies evaluated the IDS-iSYS method against the current LIAISON radioimmunoassay. Accuracy was determined by measurement of DEQAS proficiency testing samples.

Results: Imprecision of IDS-iSYS assay controls at mean concentrations of 74.4 pmol/L and 196.1 pmol/L equaled 12.0 %CV and 6.4 %CV, respectively. IDS-iSYS extraction controls at mean values of 107.0 and 233.5 pmol/L and a pooled patient sample gave CVs of 9.3%, 10.2% and 8.2%, respectively. For linearity, the maximum observed deviation from the regression line was 0.2%. Comparison of two different reagent lots showed a correlation of y=1.12 +1.17 (R=0.99). Method comparison over a range of 19.2 pmol/L to 277.2 pmol/L for the IDS-iSYS method (y) against the current LIAISON radioimmunoassay (n=28) demonstrated a correlation of y= 0.69x+16.99 (R=0.79). Measurement of DEQAS proficiency testing samples yielded a range of recovery of 99.3% to 111.6%.

Conclusions: The IDS-iSYS assay exhibited acceptable precision, linearity and accuracy and showed a moderate correlation with the LIAISON method, providing a feasible alternative to radioimmunoassay.

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Raising the bar for postvasectomy spermograms: a new high-sensitivity method by cytometry

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Objectives: Literature reports DNA-proven fatherhood after vasectomy even if persistently negative semen examinations are obtained. This shows that the post-vasectomy spermogram by microscopy generates false negatives. Our objective was to develop a quantitative, objective and highly sensitive method to determine vasectomy success.

Design and Methods: This method is a multiparametric flow cytometry analysis. It determines spermatozoa (spz) concentration and spz viability. Leukocytes (WBC) concentration is determined to detect a possible infection following the surgery.

Results: Limit of quantification for spz concentration is 200 spz/ml (dead or alive) and is 5000 WBC/ml for WBCs. Linearity for spz concentration ranges from $1x10^3$ to $1x10^6$ spz/ml (R^2>0,99) and from $1x10^4$ to $1x10^6$ WBC/ml (R^2>0,99) for WBCs. Compared to motility, viability can be detected for 5h. Duplicates have produced less than 20% variation even at the lowest concentrations. This variation is caused by the extreme rarity of the cells. Here, we report the case of a vasectomized man, who had stopped contraception after vasectomy success was confirmed by microscopy. His spouse became pregnant after 3 months of unprotected sexual relations. Two additional controls by microscopy confirmed the absence of spermatozoa. The flow cytometry method has measured a concentration of 6400 spz/ml of which 4900 spz/ml were alive. These results provided a clinical explanation and a psychological relief for the couple.

Conclusions: Although microscopic evaluation of the sample is still performed prior to cytometry to follow the guidelines, post-vasectomy spermogram by flow cytometry has now became Nasci's trusted post-vasectomy confirmation test before contraception is abandoned.

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Identification of Salicyclate Interference with Chloride ISE Using a Laboratory Data-Derived Machine Learning Algorithm

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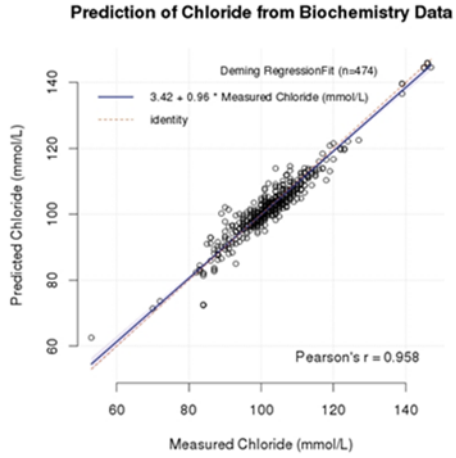
Objectives: Some chloride electrodes (e.g. Vista 1500) are sensitive to salicylate interference. High salicylate values falsely increase chloride, masking the typically elevated anion gap and delaying diagnosis and treatment. The objectives of this study were: 1) to use commonly available laboratory data to develop an algorithm to predict chloride concentrations 2) determine the performance of the algorithm at detecting salicylate interference.

Design and Methods: LIS data was used to develop a random forest regression model to predict chloride results. The algorithm was trained using known chloride concentrations with commonly available biochemistry results (CHEM-7). Data included 2876 result sets (80% for model training, 20% for testing) from 1642 patients. The chloride prediction algorithm was applied to samples with known salicylate interference to determine how well it detected inaccurate results; error detection was based on the difference between observed and predicted chloride.

Results: The most important predictors were sodium, total carbon dioxide, glucose, and potassium. At a cutoff of 1.3 mmol/L for the difference between predicted and observed chloride, the algorithm detected

high salicylate (>3 mmol/L) samples (n=12) with a sensitivity of 87% and specificity 100%.

Conclusions: The model described herein represents a new quality tool whereby predicted chloride concentrations could be used to prevent reporting inaccurate results due to salicylate interference.



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Inverse association between soluble vascular adhesion molecule-1 and soluble receptor for advanced glycation end products

Eric McNair U of Saskatchewan

Objectives : Interaction of the receptors for advanced glycation end products (RAGE) with advanced glycation end products (AGEs) results in the expression of inflammatory mediators (tumor necrosis factor-alpha [TNF-α] and soluble vascular adhesion molecule-1 [sVCAM-1], activation of nuclear factor Kappa B, and the induction of oxidative stress. All have been implicated in the development of atherosclerosis. Soluble RAGE (sRAGE) acts as a decoy for the RAGE ligand and is protective against atherosclerosis. This study aims to determine whether the levels of serum sRAGE are lower and whether the levels of serum sVCAM-1, are higher in non-ST- segment elevation myocardial infarction (NSTEMI) patients as compared to healthy control subjects.

Design and Methods: Our clinical, prospective, observational study investigated the serum levels of sRAGE, AGEs, and sVCAM-1 in a population of 50 men with NSTEMI and 50 age-and sex-matched control subjects. Serum samples were analyzed by ELISA (R&D systems, Burlington, ON) according to the manufacturer's instructions.

Results: Serum sRAGE levels were significantly lower ($p<0.001$) in NSTEMI patients (952 ± 55 pg/mL) as compared to control subjects (1287 ± 51.5 pg/mL). The serum levels of AGEs in NSTEMI patients were significantly higher than in control subjects (1192.5 ± 82.6 ng/mL versus 670.4 ± 48.8 ng/mL, $p<0.001$) and the levels of sVCAM-1 were significantly higher in NSTEMI patients as compared to control subjects (1063.8 ± 56.3 ng/mL versus 670.3 ± 45.2 ng/mL, $p=0.003$).

Conclusion: Increased **s**erum levels of age and SVCAM-1 have been reported in patients with CAD. The inverse relationship between AGE, SVCAM-1 and sRAGE in our study may indicate a potential protective effect of high levels of sRAGE against CVD.

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Hemodialysis induced release in plasma cell free hemoglobin as a source of catalytic iron in patients with End Stage Renal Disease

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Objective: Catalytic Iron (CI) is defined as nontransferrin bound iron capable of generating toxic reactive oxygen species. We have reported CI as biomarker of cardiovascular disease, associated with acute cardiac and renal injury. It is associated with adverse cardiac events specially mortality (Suhas S et al, Am Heart J, 2013). We have shown that patients on maintenance hemodialysis (MHD) having coronary artery disease have high CI (Rajapurkar, R. et al, Indian J Nephrol, 2013). Pump injury of RBCs in hemodialysis may release cell free hemoglobin (fHb) in plasma, which may contribute to the generation of CI. Aim of the present study was to measure fHb and CI in pre and post dialysis plasma sample to observe association of fHb with CI.

Design and Methods: Seventy patients on MHD, stable for at least 6 months were enrolled. Pre and post HD blood was collected in heparin; plasma was immediately separated and stored at -70^{0}C. The CI was measured by modified Bleomycin detectable iron assay (Dylan S et al. Clin Cardiol 2013) with intra and inter assay imprecision (CV) were 1.22% and 3.42% respectively. Plasma fHb levels were estimated by a highly sensitive ELISA kit (Cat No: MBS 564144, My Biosource, USA). At a plasma fHB level of 10 mg/dl the inter and intra assay CV of the kit was 0.12% and0.09% respectively.

Results: The mean pre dialysis plasma level of CI and fHB in patients were 1.66 ± 0.65 µmol/l and 5.02 ± 0.53 mg/dl. The post dialysis level of CI and fHB were 3.03 ± 1.04 umol/l and 10.51 ± 1.02 mg/dl which were significantly higher ($p<0.0001$) than the corresponding pre dialysis plasma levels. There was a significant positive correlation ($R = 0.28$, $p=0.018$) between the levels of the plasma CI and fHb in post dialysis samples.

Conclusion: Our study shows that fHb and CI significantly increases after hemodialysis. The dialysis induced fHb may contribute to the generation of CI in patients on MHD. Pump injury to RBCs appears to be the cause for this rise in fHb and CI.

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Simultaneous measurement of three anticonvulsants by high performance liquid chromatography coupled to tandem mass spectrometry

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Objectives: The measurement of lamotrigine, levetiracetam and topiramate (three new generation anticonvulsants) in the serum of patients under treatment is useful for adjusting the dosage of the molecules in their therapeutic range. To this end, we have developed and validated a method for the simultaneous determination of lamotrigine , levetiracetam and topiramate by high performance liquid chromatography (HPLC) coupled to tandem mass spectrometry (MS/MS).

Design and Methods: After proteins precipitation with methanol, the three serum compounds were separated by HPLC on Kinetex XB-C18 column, and eluted in methanol gradient (20-90%). The molecules were then detected by MS/MS following their positive ionisation by electrospray.

Results: Recovery after extraction was greater than 87% for all three molecules and their internal standard. Ion suppression was lower than 10% and carryover was insignificant. The method was linear between 0.08 and 40 µg/mL for lamotrigine, between 1 and 120 µg/mL for levetiracetam, and between 0.25 and 60 µg/mL for topiramate. Below and within the therapeutic ranges of three anticonvulsants, intra-run imprecision was less than 5% and inter-run imprecision was less than 8%. The method accuracy was 94-104% for all three molecules.

Conclusions: This HPLC-MS/MS method allows the simultaneous measurement of three anticonvulsants commonly used for the treatment of epilepsy. In addition, it is simple and fast, and is now established as routine test at Notre-Dame Hospital (CHUM), for the determination of levetiracetam and topiramate.

Abstracts

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Measurement of 3-methoxytyramine by high performance liquid chromatography coupled to tandem mass spectrometry

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Objectives: Unlike the majority of pheochromocytomas and paraglangliomas, rare dopamine-secreting tumors (usually paraganglioma) cannot be diagnosed by measurement of catecholamines and metanephrines in urine and plasma. However, the diagnosis could be established using 3-methoxytyramine (3-MT), a dopamine metabolite. Its quantification in plasma could identify some inherited forms of metastatic paraganglioma. Hence, we have developed and validated a measurement method of 3-MT by high performance liquid chromatography coupled to tandem mass spectrometry (HPLC-MS/MS) with solid phase extraction (SPE) online automated.

Design and Methods: The assay was performed on the Symbiosis system (Spark Holland) coupled to Quattro Premier (Waters) with electrospray positive ionization. Plasma samples were injected and extracted using SPE cartridges, and automatically routed to HPLC separation on Atlantis HILIC silica column (3µm, 100Å, 50x4.6mm, Waters) using a linear gradient (ammonium formate-acetonitrile). 3-MT was identified and quantified by MS/MS.

Results: The method is linear from 0.048 to 24.55 nmol/L, with a limit of detection of 0.012 nmol/L and a limit of quantitation of 0.048 nmol/L. No carryover was observed (0.10%). Recovery was 93.0±1.5% and matrix effect of 128-160% was observed but compensated by the internal standard (3-MT-d4). Within-run and between-run CVs were 3.7-7.7% and 2.3-13.8%, respectively. Quantification of 29 frozen samples from external quality control program showed an excellent correlation between our results and assigned values.

Conclusions: This measurement method of 3-MT by SPE-LC-MS/MS is simple, fast and is being implemented as routine test at Saint -Luc hospital (CHUM) for the diagnosis several hereditary and malignant forms paragangliomas.

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A comprehensive LC/MS assay for biogenic amines in urine

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Objective: to develop an LC/MS assay for the commonly tested urine biogenic amines *i.e.* vanillylmandelic acid (VMA), hydroxyindoleacetic acid (HIAA), homovanillic acid (HVA), epinephrine, norepinephrine, dopamine, metanephrine (MET) and normetanephrine (NMET).

Design and Methods: urine is precipitated with acetonitrile containing internal standards, following which the evaporated supernatant is treated with sodium cyanoborohydride and deuterated acetaldehyde. The solution is diluted with water and analyzed by reverse-phase LC/MS. Free, rather than total, MET/NMET are measured.

Results: using a basic LC/MS instrument, the assay can measure elevated levels of all compounds in 5L/d urine at 5.5 min between injections. Between-run precision for commercial low-level QC ranged from 4.0-8.1% for all compounds except epinephrine (14.8%). Correlations with existing methods for catecholamines (LC/ECD) and other compounds (LC/MS) showed slopes of 1.00±0.1 and $r^2 \geq 0.89$, the exceptions being epinephrine (due to insensitivity of LC/ECD) and MET/NMET (free vs total assays). Reference ranges (97.5th percentile), developed from patients presumably being investigated for secondary hypertension, were epinephrine (<90 nmol/d), norepinephrine (<650 nmol/d), dopamine (<3300 nmol/d), free MET (<0.2 umol/d) and free NMET (<0.4 umol/d). Reference ranges (97.5th percentile) from patients on whom VMA or HIAA had been requested, were <38 umol/d and <50 umol/d, respectively. Marked elevations of free MET/NMET were observed for 3 patients with suspected adrenal tumours.

Conclusions: a single LC/MS assay can quantitate all common biogenic amines.

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Pediatric reference value distributions for vitamins A and E in healthy community children: Establishment of new age-stratified reference intervals from a CALIPER cohort

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Objective: A challenge of vitamin A (retinol) and E (alpha tocopherol) testing is lack of reliable pediatric reference intervals (RI). We report new RI in healthy children for vitamin A & E as part of the Canadian Laboratory Initiative for Pediatric Reference Intervals (CALIPER).

Methods: Healthy community children were recruited and whole blood samples collected from 342 healthy children 1 day to 19 years of age. Serum retinol and a-tocopherol were measured by HPLC. Age and sex-specific RI were calculated based on CLSI C28-A2.

Results: Comparison of vitamin A and E levels in males and females demonstrated a tight correlation and did not reveal any significant sex related differences. Further analysis by age demonstrated distinct partitioning patterns. Both vitamin A and E showed age partitioning at 0 to <1 years with levels present as early as the first day of life. Vitamin A exhibited a complex pattern necessitating 4 distinct age partitions trending toward a general rise in levels with increasing age. Vitamin E required 2 age partitions. Levels rose within the first year of life but were reduced slightly after this period requiring only one broad partition between 1 to <19 years. Ratios of vitamin E to cholesterol and triglyceride were also calculated, and correlated well to vitamin E levels.

Conclusions: This study establishes pediatric RI for vitamin A and E in a healthy population of children from neonates to early adulthood. These values will be beneficial in assessing accurate vitamin status when monitoring children with GI disorders or malnutrition.

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Impact of improved glucose monitoring in the neonatal intensive care unit: an evaluation of analytical and clinical performance of the point of care Nova Statstrip

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Objective: To evaluate the analytical and clinical performance of new glucose point of care testing (POCT) devices implemented into a neonatal intensive care (NICU) setting.

Methods: Analytical performance of the Nova StatStrip and SureStep Flexx meters were assessed and compared. Clinical outcomes were evaluated in 490 patients admitted to the NICU including rate of hypoglycemia and clinical sensitivity/specificity for detecting critical results.

Results: Imprecision using control material (2.8-15.7 mmol/L, n=20) and pooled patient specimens (5.1-23.7 mmol/L, n=20) were <8% CV for SureStep, and <5% CV for Nova. Method comparison to Ortho Vitro950 (n=120) revealed correlations of y=0.867x+0.82 (R=0.990) for SureStep, and y=1.016x+0.04 (R=0.997) for Nova. Studies to assess clinical performance of Nova revealed fewer readings per visit (24%, p=0.001) in NICU patients compared to SureStep. This was associated with a trend towards reduction in frequency of hypoglycemia ≤2.2 mmol/L (53%, p=0.053) as well as critically low ≤3.0 mmol/L (35%, p=0.112) and high results ≥9.0 mmol/L (40%, p=0.009). The sensitivity/specificity for detecting critically low results was 70.2/98.7% and 80/99.5% for SureStep and Nova, respectively. Clinical comparisons demonstrated correlations of y=0.983x+0.24 (R=0.931) for Nova (n=607) and y=1.1x-0.036 (R=0.869) for SureStep (n=977) compared to lab values.

Conclusions: The Nova StatStrip meter demonstrated superior analytical precision and accuracy compared to SureStep. This was associated with improved sensitivity and specificity for detection of critical glucose results, translating into better quality of care in the NICU.

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Automated chemiluminescent immunoassays for measurement of plasma renin: A method comparison versus radioimmunoassay

Joshua Raizman, Paul Yip, Vathany Kulasingam

Objectives: To evaluate the analytical performance of the automated DiaSorin LIAISON and IDS-iSYS immunoassays for measurement of human plasma renin.

Design and Methods: Precision was evaluated using LIAISON or IDS-iSYS controls and patient pooled samples. Linearity across the measuring range was assessed using patient samples. Method comparison studies were evaluated against the CISBIO Renin III Generation radioimmunometric assay (RIA).

Results: Imprecision of LIAISON control 1 and 2 at mean values of 13.8 and 54.8 ng/L equaled 3.7 %CV and 4.7 %CV, respectively, while CVs of IDS-iSYS control 1, 2, and 3 at mean values of 9.4, 61.1, and 248.9 ng/L equaled 6.3%, 8.1%, and 8.7%, respectively. Patient pools on the LIAISON at mean concentrations of 5.8, 93.6, and 275.2 ng/L gave CVs of 7.8%, 6.3%, and 3.9%, respectively, while patient pools on the ISYS at mean concentrations of 8.1, 110.6, and 307 ng/L gave CVs of 10.8%, 9%, and 4.2%, respectively. Linearity across the measuring range for both methods was verified with systematic errors <6%. Method comparison studies on the LIAISON (n=62) and iSYS (n=61) against the current RIA method demonstrated correlations of y=1.506x-11.6 (R=0.9681) with a mean bias of +15.6 ng/L, and y=1.508x-7.4 (R=0.9734) with a mean bias of +20.4 ng/L, respectively. Comparison of LIAISON and iSYS (n=59) demonstrated a closer correlation of y=1.032x+3.2 (R=0.9915) with iSYS having a mean bias of +5.3 ng/L.

Conclusions: The LIAISON and iSYS renin assays are fully automated assays with acceptable performance that will assist in clinical assessment of hypertensive patients.

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Aldosterone Testing: Evaluation of serum and urine applications on the DiaSorin LIAISON automated chemiluminescent analyzer

Joshua Raizman, Paul Yip, Vathany Kulasingam

Objectives: To evaluate the analytical performance of the automated DiaSorin LIAISON aldosterone immunoassay for measurement of serum and urine.

Design and Methods: Precision was evaluated using LIAISON controls and patient pooled samples. Linearity across the measuring range was assessed using diluted patient samples while accuracy was assessed with spiking-in studies using purified aldosterone and proficiency testing (PT) materials. Method comparison of serum or urine samples on the LIAISON were evaluated against either the current Siemens (DPC) radioimmunometric assay (RIA), the IDS-iSYS immunoassay, or an LC-MS/MS method.

Results: Imprecision of LIAISON (n=20) Low and High controls at mean values of 150 and 784 pmol/L equaled 10.8 %CV and 6.6 %CV, respectively, agreeing with the manufacturer's claimed precision. Patient pools at mean concentrations of 234, 889, and 2258 pmol/L gave CVs of 9%, 4.3%, and 4.4%, respectively. Linearity was verified across the measuring range (83-2770 pmol/L). Method comparison studies of serum samples on the LIAISON over the range of 192-2624 pmol/L against the current RIA method and IDS-iSYS (n=41) demonstrated correlations of y=1.45x-152 (R=0.916) and y=1.181x-78.9 (R=0.971), respectively. For urine, method comparison of LIAISON against LC-MS/MS (n=40) demonstrated a correlation of y=0.869x+176.26 (R=0.9917). For the spiking-in study, percent recoveries were 98-111%. Analysis of PT material demonstrated comparable values to the Diasorin peer group results based on a limited number of participants.

Conclusions: The LIAISON aldosterone assays demonstrated acceptable performance and should provide reliable serum and urine aldosterone measurements in the assessment of hypertensive patients.

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Establishment of pediatric reference intervals for galectin-3 on the Abbott ARCHITECT using healthy community children from the CALIPER study

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Objectives: As growth and development can markedly influence normal circulating concentrations of analytes, establishment of accurate reference intervals for the pediatric population has become indispensable for many clinical chemistry tests. The CALIPER study is aimed at establishing the influence of age, gender, and pubertal stage-specific changes on biochemical markers in a healthy, non-hospitalized population to develop a comprehensive database of pediatric reference intervals. We therefore sought to establish the pediatric reference interval (RI) for galectin-3, which plays important regulatory roles in inflammation, immunity and cancer.

Design and Methods: A total of 354 samples from ethnically diverse healthy community children aged one day to 18 years were collected and analyzed on the Abbott ARCHITECT i2000SR. Following the CLSI C28-A3 guidelines, age- and sex-specific partitioning was determined for galectin-3 analyte. Non-parametric and robust methods were used to establish the 2.5th and 97.5th percentiles for the galectin-3 RI as well as the 90% confidence intervals. Abbott galectin-3 quality control material was used to determine between day precision.

Results: Precision of the galectin-3 assay was <6% (level#1(n=21) mean=8.7ug/L, CV=5.3%; level#2(n=20) mean=18.9ug/L, CV=2.9%; level#3(n=20) mean=71.2ug/L, CV=2.0%). A significant age-specific difference in galectin-3 appears for newborns (<6 days old, RI= 13.7 (90%CI: 12.4-15.2) to 59.1 (90%CI: 44.3-72.2)) and those between 6 days to <19 years of age (RI= 6.5 (90%CI: 5.1-7.0) to 23.3 (90%CI: 20.2-31.5)).

Conclusions*:* This study establishes the pediatric RI for galectin-3 on the Abbott ARCHITECT platform. This new RI will need to be validated in other populations and for other immunoassay platforms.

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Reactivity of macroprolactin in two widely used commercial prolactin immunoassays

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Objectives: Prolactin (PRL) hypersecretion may lead to hyperprolactinemia. Approximately 15-26% of hyperprolactinemic patients have macroprolactin, which is a PRL-immunoglobulin complex. Previously it has been shown that macroprolactin has variable detection by different immunoassays. One accepted method for detecting macroprolactinemia is polyethyleneglycol (PEG) precipitation. The objective of this study was to evaluate the performance of the PEG-precipitated PRL samples on the Abbott ARCHITECT compared to Roche E170.

Design and Methods: Sera (n=20) submitted for macroprolactin evaluation were used to compare macroprolactin interference on the Abbott ARCHITECT and Roche E170. A second group of randomly selected samples (n=40) was used to compare the PRL as a part of the validation of the Abbott method.

Results: PRL results from macroprolactin samples ranged from 10.6 to 93.5 ug/L and 4.8 to 74.9 ug/L for post-PEG precipitation monomeric PRL. The Passing-Bablok analysis of macroprolactin by the Abbott ARCHITECT and Roche E170 yielded a constant bias of -2.27, with a significant proportional bias of 1.37. Comparison analysis of PEG-precipitated samples resulted in the regression equation with a slope of 1.09 and an intercept of 0.52, which was similar to the random group of samples ($y = 1.07x + 1.22$).

Conclusions: Our data suggest that macroprolactin interference with the Abbott method is greater than that seen on the Roche method. This confirms that assays from different manufactures give variable prolactin results in the presence of macroprolactin. This reinforces the necessity of screening for macroprolactin in hyperprolactinemic patients in order to avoid misleading diagnoses.

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Evaluation of a fluorometric method for semi-quantitative determination of biotinidase activity in newborn dried bloodspots on the Wallac VICTOR2 automated platform and establishment of biotinidase stability and reference intervals

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Objectives: Evaluation of Perkin Elmer neonatal biotinidase kit for use on the VICTOR^{2TM} fluorometer and establishment of biotinidase stability and reference intervals.

Design and Methods: The neonatal biotinidase kit was evaluated for precision, linearity, accuracy, analytical sensitivity, and interference on the VICTOR^{2TM} fluorometer. Precision experiment ran abnormal and normal QC material over 20 working days (n=39). Linearity included six levels run in triplicate. Comparison studies (n=3756) were conducted between a manual, colorimetric, method and an automated, fluorometric method. Instrument to instrument comparison (n=1102) was made between two VICTOR^{2TM} fluorometers. Dried bloodspot biotinidase stability was examined and reference intervals were established (n=2920) using a non-parametric, percentile rank method.

Results: The fluorometric neonatal biotinidase method demonstrates acceptable within-run (L1=56, CV=10%; L2=283, CV=10%) and between-run precision (L1=56, CV=11%; L2=283, CV=11%) and analytical measurement range (5-400U, U=nmol/min/dL). The manual colorimetric and automated fluorometric methods show 87% agreement and high discrepancy in the borderline range. The VICTOR platforms correlate strongly (R^2=0.982, y=0.999x-2.86, bias=2.2%). The functional sensitivity is 4.9U. Bilirubin interference (-21% difference) was observed between a normal biotinidase activity sample without bilirubin (346U) and the same sample with 500umol/L bilirubin (289U). Dried bloodspot biotinidase stability was acceptable at room temperature for 12 days. Normal, borderline and deficient biotinidase activity cut-offs of >45U, 20-45U and <20U, respectively were established for Alberta newborns.

Conclusions: The neonatal biotinidase kit performance is satisfactory for screening newborn dried bloodspots on the VICTOR^{2TM}. Clinical laboratories should be aware of bilirubin interference, discrepancy in the borderline range and establish their own reference intervals.

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Assessment of galectin-3, N-terminal pro-brain natriuretic peptide and inflammatory cytokines in patients with myocardial injury after initiation of adjuvant trastuzumab therapy

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Objectives: Detection of myocardial injury following anthracycline-containing chemotherapy regimens but prior to trastuzumab in patients receiving adjuvant therapy for HER2 positive breast cancer is being investigated. The aim of this study is to assess if serum levels of biomarkers related to heart failure (HF: N-terminal pro-brain natriuretic peptide (NT-proBNP), interleukin-6 (IL-6), monocyte chemotactic protein-1 (MCP-1), and galectin-3), would be increased following three cycles of trastuzumab in patients with myocardial injury present before trastuzumab treatment initiation.

Design and Methods: Of the ten patients enrolled in our pilot study (Clin Chem 2013;59:327-329), five had evidence of myocardial injury (hsTn>99th percentile) before trastuzumab treatment. EDTA plasma was obtained after each of the first four cycles of trastuzumab therapy, using cycles 2-4, NTproBNP (Roche E-modular), galectin-3 (Abbott ARCHITECT), and IL-6, MCP-1 (Randox Evidence Investigator) were measured. The following cutoffs based on health-outcome studies assessing HF were used to determine the prevalence of abnormal concentrations over this timeframe: galectin-3>17.8ug/L or >15% increase from end of first-round of treatment (Circ Heart Fail 2013;6:219-26), NT-proBNP>183ng/L, IL-6>6.4 ng/L, and MCP-1>156ng/L (Clin Chem 2007;53:2112-2118).

Results: Of 15 serum samples collected after initiation of trastuzumab from 5 patients with evidence of myocardial injury (median hsTnI=47 ng/L; hsTnT=22 ng/L), all galectin-3 results were <17.8 ug/L with no samples exhibiting a significant increase (all <15%). Whereas, 20%, 40%, and 60% of results for IL-6, NT-proBNP, and MCP-1 were abnormal.

Conclusions*:* Additional research investigating biomarker levels in women with trastuzumab-mediated decrease in left ventricular ejection fraction is required for selecting optimal HF biomarkers.

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Prevalence of known and unknown diabetes in emergency department patients presenting with symptoms of acute coronary syndrome

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Objectives: We sought to determine the prevalence of self-reported/physician documented diabetes versus those with only an abnormal laboratory biochemical result (i.e., elevated concentration of HbA1c and/or glucose) in patients who had a cardiac troponin ordered by an emergency department (ED) physician and had symptoms of acute coronary syndrome (ACS).

Design and Methods: Following research ethics board approval, over a period of one month, we measured at ED presentation plasma glucose (Abbott ARCHITECT) and retrospectively HbA1c (whole blood; filter paper method, *Clin Chem*2011;57:577-85) from consecutive patients who had a cardiac troponin ordered by an ED physician. The presence of diabetes was obtained via research assistant facilitated patient interview/physician documentation or via measurement of HbA1c (blinded to physicians) and glucose using cutoffs endorsed by the Canadian Diabetes Association (i.e., HbA1c≥6.5%; glucose≥11.1 mmol/L for random sample). Descriptive statistics were performed via Statsdirect software.

Results: There were 599 patients (median age(interquartile range)=68y (56-78); 54.4% male) with 30.6%(95%CI:26.9-34.4) of patients having documented diabetes and 4.7% (95%CI:3.1-6.7) of patients with HbA1c≥6.5% and no documented diabetes. Addition of glucose to HbA1c did not significantly raise the prevalence in the biochemically identified diabetic group (5.3% (95%CI:3.8-7.5)). The prevalence of HbA1c≥6.5% in patients being evaluated for ACS was significantly higher than the prevalence of HbA1c≥6.5% in a general ED population with no documented diabetes (i.e., 1.9% (95%CI:1.2-2.9) *BMJ Open* 2013; 3: e003411.)

Conclusion: Targeted screening for diabetes in ED patients with ACS symptoms with HbA1c appears to identify more diabetic patients than applying this in a general ED population.

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On-board stability of QC materials on Siemens Vista 1500® analyzer

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Objectives: To verify the on-board stability of QC materials on Siemens Vista 1500®.

Design and Methods: Sufficient quantities of Bio-Rad (Hercules, CA) Multiqual Unassayed® QC materials were prepared to test 35 analytes (15 chemistry, 3 electrolytes, 3 lipids, 8 enzymes, 6 drugs) in triplicate from on-board and off-board processes. Materials were analyzed on day 0 as baseline and, for additional eight days, triplicate analysis was performed from the vials kept on-board (2-8°C) and from aliquots of QC material kept off-board in refrigerator (2-8°C). No additional QC materials

were prepared or loaded for the duration of the experiment. On-board stability was accepted in following conditions: 1) *p* values from *t*-test for means and *F*-test for variances of both on- and off-board procedures were equal or greater than 0.05; 2) if *t*-test *p* value is less than 0.05 but average daily bias (on-board) against day 0 was less than 1 SD; 3) if the *F*-test *p* value is less than 0.05, but the on-board imprecision is less than off-board imprecision or precision goal. Data were analyzed using Microsoft Excel®.

Results: 21 analytes passed both t-test and F-test. 10 analytes (bicarbonate, ethanol, iron, Mg, protein, HDLC, GGT, lipase, carbamazepine, phenytoin) failed t-Test but the on-board bias was less than 1SD. 7 analytes (TIBC, total cholesterol, ALT, AST, lipase, carbamazepine, phenytoin) failed F-test but the on-board imprecision was less than off-board precision or precision goal.

Conclusions: All 35 analytes in QC materials were stable on-board for at least eight days for daily QC practice.

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Transient early increase in thyroglobulin levels post-radioiodine ablation in patients with differentiated thyroid cancer

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Objectives: Treating differentiated thyroid cancer (DTC) includes surgical thyroidectomy and, in most cases, radioiodine (RAI) ablation. Measurement of serum thyroglobulin (Tg) level is used for assessing disease burden and for identifying persistent-recurrent DTC. Recent observation has shown that Tg levels are elevated shortly after RAI-ablation, which may be misinterpreted as extensive disease depending on timing of blood sampling. Thus, this prospective study aims to determine the Tg profile before and after RAI-ablation in DTC patients.

Design and Methods: Fifty-five DTC patients (without known residual/metastatic disease following thyroidectomy) received RAI-ablation (I-131 median dose 2.2 GBq). Blood specimens collected at baseline (n=54), pre-ablation (n=55), one week post-ablation (n=55) and at six months (n=39) were assayed for Tg levels. Pre- and post-ablation Tg measurements followed brief (3 weeks) thyroid hormone withdrawal to achieve serum TSH ≥30 mU/L. Tg was measured by Roche-Cobas ECL-immunoassay (sensitivity=0.8 µg/L). Thyroid remnant size was estimated from whole body scintigraphy performed after RAI-ablation.

Results: Mean Tg levels at baseline and pre-RAI were 5.1 µg/L and 13.7 µg/L, respectively (*p=ns*). At one week post-RAI, the mean Tg increased approximately 13-fold to 175.5 µg/L (*p<0.001*). There was a weak, but statistically significant, correlation between thyroid remnant size and the absolute or relative Tg increase (*p<0.05*). By 6-months follow-up, mean Tg levels had decreased to 2.3 µg/L (*p<0.001*). None of the patients had recurrence of disease at follow-up.

Conclusions: This study confirms not only a large early increase in Tg post-RAI ablation, but that Tg levels return to baseline by 6-months. Recognizing this transient increase is important for post-ablation Tg interpretation, and likely reflects RAI-induced Tg release from the thyroid remnant.

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Dynamic changes in circulating amino acids and acylcarnitines in children and adolescents: A CALIPER study of healthy community children and new pediatric reference intervals

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Objectives: An up-to-date and comprehensive database of pediatric reference intervals (RI) is essential for the accurate management of children with metabolic disease. The Canadian Laboratory Initiative for Pediatric Reference Intervals (CALIPER) program has established pediatric RI from healthy community children for a comprehensive list of common biomarkers used in the diagnosis and management of inborn errors of metabolism (IEM).

Design and Methods: Healthy children and adolescents from birth to 19 years were recruited based on informed parental consent. A cohort of over 500 healthy individual samples was used to calculate pediatric RI for 35 acylcarnitines (LC-MS/MS) and 36 amino acids (Waters MassTrak amino acid analyzer). RI were calculated using non-parametric statistics according to CLSI-C28-A3 and partitioned based on age and sex.

Results: Of all the amino acid and acylcarnitine analytes evaluated here, 82% required 2 – 4 age-dependent RI, with 65% of all analytes producing a newborn RI of either 0 – 1 week or 0 – 2 weeks. Also, 23% of all analytes displayed a unique RI during puberty, half of which produced sex-based RI. These were often related to energy metabolism and growth in muscle, such as branched-chain amino acids and total carnitine. Finally, only 14% of analytes produced one RI for birth – 19 years.

Conclusions: The RI established here for acylcarnitines and amino acids will aid in the accurate management of children suspected of IEM. Importantly, these RI are established for the indicated instrumentation and should be validated on other platforms and for local populations as recommended by CLSI.

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An open source interval arithmetic and fraction calculator for clinical laboratory information systems

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Objectives: Some clinical laboratory test results are reported as less than or greater than the analytical measuring range. When such an interval result is required for calculations, some systems ignore the out-of-range symbol while others fail to report the calculated result. Mathematical literature typically considers only closed bounds (limits included), whereas clinical applications often require open bounds. We sought to develop an open source universal interval arithmetic calculation engine with functionality appropriate for clinical laboratory applications.

Design and Methods: In consultation with colleagues, clinicians, and mathematicians, we developed an Excel spreadsheet with user-defined Visual Basic for Applications (VBA) macro functions, listing over 500 interval arithmetic examples. Calculations that don't match expected values are automatically highlighted in red boldface for troubleshooting and validation.

Results: Our algorithm is compatible with closed or open bounds and can perform basic arithmetic, exponentiation, compute logarithms and anti-logarithms with ordinary numbers, less than or greater than values, or intervals with bounds expressed in "Lower To Upper" or in "Centre±Radius" formats.

Conclusions: We hope that commercial laboratory information systems will incorporate a universal interval arithmetic calculation engine so that every calculation in every context will be compatible with interval results. Future work will focus on establishing a web site for free exchange source code, translating it into other programming languages, and proposals to include interval arithmetic in clinical laboratory information system accreditation standards.

Abstracts

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Validation of the Abbott i-STAT total β-hCG cartridge for use in rural Alberta hospitals

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Objectives: Human chorionic gonadotropin (hCG) has significant clinical utility, yet many rural hospitals lack instrumentation for quantitative measurement. This study aimed to evaluate Abbott's new quantitative i-STAT β-hCG cartridge, as it offers a feasible option for onsite quantitative testing in rural hospitals.

Design and Methods: Linearity, imprecision and accuracy were assessed. A plasma sample (hCG=1799 IU/L) was diluted from 1/2 to 1/256 (measured in duplicate) for linearity. Two levels of Clinica (24 IU/L, 1455 IU/L) and Bio-Rad Immunoassay Plus (6 IU/L, 21 IU/L) quality controls were measured daily over 20 days for imprecision. Accuracy was assessed by measuring hCG in plasma on both the i-STAT and Siemens Dimension Vista (n=37), Beckman Coulter DxI 800 (n=39), or Roche Cobas 6000 (n=42). Whole blood samples were also measured with the i-STAT; samples were then centrifuged and plasma was measured with central lab analyzers (n=43, n=34, n=52, respectively; range <1 - 161,207 IU/L).

Results: Linearity was demonstrated (9-1799 IU/L). Total imprecision was acceptable (Bio-Rad: mean=24 IU/L, CV=7.7% and mean=21 IU/L, CV=4.4%; Clinica: mean=24 IU/L, CV=5.1% and mean=1455 IU/L, CV=3.0%). Comparison of plasma on the i-STAT yielded acceptable correlations (Vista slope=1.1105, y-intercept=9 IU/L, R^2=0.9849; DxI slope=0.9727, y-intercept=3 IU/L, R^2=0.9943; Cobas slope=1.0043, y-intercept=4 IU/L, R^2=0.9997). Whole blood sample comparisons gave similar results.

Conclusions: Performance of the i-STAT β-hCG test for whole blood and plasma was acceptable. It can be utilized in clinical settings without access to a large chemistry analyzer for quantitative hCG testing; it is specifically useful for a stat quantitative hCG result.

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SPE-LC-MS/MS Method for the Quantification of Bradykinin in Human Plasma

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Objectives: Bradykinin is intrinsically involved in blood pressure regulation and inflammatory reactions through its vasodilatory effects and ability to elevate vascular permeability. Accurate quantification of bradykinin in plasma is particularly challenging because it is present in low pg/mL levels, is rapidly metabolized, and is artificially produced via proteolytic processes. Our study utilizes specifically designed blood collection techniques to inhibit bradykinin formation *ex vivo*, solid-phase extraction and a novel LCMS System for the determination of bradykinin levels.

Methods: Human plasma was collected in BD™ P100, P700, P800 and tubes containing only K2EDTA. [Lys-des-Arg9]-Bradykinin was added to 100 µL plasma as Internal Standard (IS) and samples extracted using a mixed mode 96 well OASIS® WCX µElution plate. 10 µL of extracted sample was injected onto an iKey™ (BEH C18, 300Å, 1.7 µm) microfluidic separation device connected to a Waters ACQUITY® M-Class UPLC and a Waters Xevo® TQ-S mass spectrometer. The 354.18>419.18 transition was used for quantitation.

Results: The assay was linear (r^2>0.99, 1/X) from 2.5 - 8000 pg/mL. Mean accuracies for QCs was 92.7-104.0 with %CVs at 1.21-4.31. Sample handling is critical and the BD P700 tubes exhibited best ex vivo stability for the assay.

Conclusions: The system as presented, provides for a sensitive, robust assay for Bradykinin from human plasma with an LOD of 2.5 pg/mL.

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A patient comparison study of Epoc versus Gem 4000 and i-STAT for pH, PCO2 and pO2

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Objectives: Patient results for pH, pCO2 (mm Hg) and pO2 (mm Hg) from the new Alere epoc® Blood Analysis System (Epoc) were compared to the established IL Gem® Premier 4000 (Gem) and the Abbott i-STAT® System (i-STAT).

Design and Methods: Patient specimens (27 arterial, 4 venous) collected using Radiometer safePICO syringes were analyzed immediately on Epoc (31), Gem #1 (4), Gem #2 (11), both Gems (16) and i-STAT (9). For each analyte, the difference was calculated for each specimen: Epoc minus Gem or average Gem and Epoc minus i-STAT. The mean ± 2 SD of the differences for Epoc minus Gem and Epoc minus i-STAT was compared to acceptance limits in College of American Pathologists (CAP) proficiency testing surveys: pH ± 0.04, pCO2 ± 5 or 8% and pO2 (peer group ± 3 SD – estimated from two 2013 CAP surveys as ±12 and ±18 for Gem and i-STAT, respectively). Linear regression analysis for Epoc versus Gem and Epoc versus i-STAT was also done.

Results: The mean differences ± 2 SD and linear regression statistics for Epoc versus Gem and i-STAT are listed below.

	Epoc versus Gem			Epoc versus i-STAT		
	pH	pCO2	pO2	pH	pCO2	pO2
Mean Difference ± 2 SD	0.01 ± 0.03	0.8 ± 3.8	3.2 ± 8.2	0.00 ± 0.03	-0.4 ± 2.0	6.5 ± 6.2
Slope	0.97	0.94	1.03	1.11	1.01	1.12
y-Intercept	0.22	3.21	1.00	-0.80	-0.88	-2.14
Correlation Coefficient	0.98	0.98	0.99	0.93	1.00	0.98

Conclusions: Patient results for pH, pCO2 and pO2 from Epoc showed acceptable correlation to Gem and i-STAT.