

22nd Annual Infectious Diseases Research Day

&

9th Annual Canadian Center for Vaccinology Symposium



April 11th, 2017
Halifax

Sponsored by:

Canadian Center for Vaccinology

**Dalhousie Divisions of Infectious Diseases
of the Departments of Pediatrics and Medicine**

Dalhousie Infectious Diseases Research Alliance

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Welcome to the 22nd Annual Infectious Diseases Research Day and 9th Annual CCfV Symposium!



Shelly McNeil MD, FRCPC
Chief
Div of Infectious Diseases,
Dept of Medicine, Dalhousie

We are pleased to announce that the program for the 2017 Research Day is as comprehensive as ever! A variety of poster and oral presentations cover the wide area of infectious disease from bench science to observational KABB studies.

The research presented at our conference is conducted by highly experienced investigators, mentoring top-notch graduate and post-graduate trainees along with skilled technicians, analysts, and support staff to ensure that research is developed and executed at the highest standard. Our annual research day is an opportunity for the research community to showcase their hard work to both peers and public. Evaluation of the research presented at this event is extremely important: you will receive an email inviting you to take our post event survey and we urge you to give us your feedback so we can continue to improve upon this learning event for all involved.



Scott Halperin MD, FRCPC
Director
Canadian Center for
Vaccinology

You will notice that we have condensed this year's meeting into one full day: this decision was made with the intent to enhance the experience of our attendees and provide a more accommodating schedule. The entire program has been amalgamated into one streamlined day of oral and poster presentations, keynote lectures, and a timely panel on infectious diseases outbreaks and different perspectives from public health, physicians, and community members.

We encourage everyone to make the most of this educational experience, and relish the exposure to new and exciting research happening at Dalhousie and beyond.

Our sincere thanks to the dedicated planning committee and the financial support from our corporate sponsors, both of which make this educational opportunity possible.

Program

22nd Annual Infectious Diseases Research Day &
9th Annual Canadian Center for Vaccinology Symposium

Tuesday April 11, 2017

8:00-9:00am	TJ Marrie Lecture- Dr. Andrea Cox, <i>HCV: Next on the list for eradication?</i>	Halifax Infirmary RB Theatre
9:30-12:30pm	Oral Presentations (10)	Dalhousie University MacInnes Room
12:30-1:15pm	Lunch	
1:00-2:00pm	Presentation – Shelley Deeks, <i>Vaccine Pharmacovigilance - Strength in Numbers</i>	
2:00-2:30pm	Presentation – Paul Bonnar, <i>Behavioural change interventions to improve antimicrobial prescribing</i>	
2:30-3:00pm	Presentation – Lisa Barrett, <i>Eager for Elimination: learning from HCV cure</i>	
3:00-4:00pm	Poster judging (posters on display 1:00 – 5:00)	Dalhousie University MacInnes Room Foyer
4:00-5:00pm	Panel: <i>Perspectives on Outbreaks of Vaccine Preventable Diseases in Canada</i> Shelly McNeil Trevor Arnason Noella Whelan George Worthen	Dalhousie University MacInnes Room
5:00-5:30pm	Awards and closing remarks	

Educationally co-sponsored by Dalhousie University Continuing Professional Development

This program is supported by contributions from Sanofi Pasteur, Merck, Pfizer, Astellas, and Gilead



Speakers



Dr. Andrea Cox is currently a Professor of Medicine and Oncology at the Johns Hopkins School of Medicine. She earned her Ph.D. studying T cell immunology at the University of Virginia. She subsequently completed an MD and Internal Medicine and Infectious Disease training at Johns Hopkins. Clinically, she specializes in the treatment of patients with hepatitis virus infections. Her laboratory investigates human immune responses to HCV, HBV, and HIV, including mechanisms through which these chronic viral infections stimulate and evade immune responses and HCV vaccine development. She has been an active participant in clinical trials of direct-acting antivirals for the treatment of hepatitis C virus. She is a principal investigator on the first prophylactic HCV vaccine trial ever implemented in at-risk people.



Dr. Shelley Deeks is the Medical Director of Communicable Diseases, Emergency Preparedness and Response at Public Health Ontario and an Associate Professor at the Dalla Lana School of Public Health, University of Toronto. She is a member of Canada's National Advisory Committee on Immunization, Scientific Lead of Ontario's Provincial Infectious Diseases Advisory Committee on Immunization and past Chair of the World Health Organization's Immunization Practices Advisory Committee. Dr. Deeks holds Fellowships in Public Health in both Canada and Australia.



Dr. Lisa Barrett is an Assistant Professor in the Division of Infectious Diseases and Department of Microbiology and Immunology at Dalhousie University in Halifax. She is Royal College certified in Internal Medicine and Infectious Disease and is also a viral immunologist studying chronic viral infection. She utilizes hepatitis C and HIV treatment and cure to study immune aging, as well as models of health care delivery that support disease elimination.



Dr. Paul Bonnar completed his Internal Medicine and Infectious Diseases training at Dalhousie University. He is currently completing a clinical fellowship in Antimicrobial Stewardship at the Sinai Health System – University Health Network Antimicrobial Stewardship Program. After completing this fellowship, Paul will be the physician co-lead for the NSHA antimicrobial stewardship program.

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(Presenter's name in **bold**)

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Abstracts

(Presenter's name in **bold**)

1. MULTITARGET PLASMID CONTROLS FOR CONVENTIONAL AND REAL-TIME PCR-BASED SEROTYPING OF *STREPTOCOCCUS PNEUMONIAE*

Authors: J Schembri¹, H Gillis¹, M Warhuus¹, S McNeil¹, J LeBlanc¹

Affiliation: ¹Canadian Center for Vaccinology (CCfV), IWK Health Centre, and Nova Scotia Health Authority (NSHA), Dalhousie University, Halifax, NS, Canada

Introduction: Serotyping of *Streptococcus pneumoniae* is an integral part of disease surveillance, and over 90 serotypes have been characterized by traditional serotyping methods (Quellung reaction). Molecular serotyping methods for *S. pneumoniae* are now increasingly being used that rely on conventional multiplex PCR (cmPCR) and real-time multiplex PCR (rmPCR). Given that cmPCR consist of 8 multiplex reactions with 40 targets, and rmPCR consists of 7 triplex reactions, generating positive controls for these assays can be challenging. This study designed and evaluated two plasmids controls: a 43-target plasmid for cmPCR (pSpn-CM1) and a 23-target plasmid for rmPCR (pSpn-RM1).

Methods: Each plasmid was designed and synthesized as chimeric DNA sequences with all target primer binding sites sequences, as well as probe binding sites in pSpn-RM1. Additional targets (*lytA* and *cpsA*) were included in both pSpn-CM1 and pSpn-RM1 for quantification following propagation and purification in *Escherichia coli*. The pSpn-CM1 and pSpn-RM1 plasmids were tested against each cmPCR and rmPCR reaction respectively.

Results: When tested using the cmPCR reactions, all targets of expected band sizes (including the *cpsA* internal control) could be amplified reproducibly from pSpn-CM1 with good amplicon visibility at a concentration of 10⁴ copies/μl. For the rmPCR reactions, all targets were reproducibly amplified with pSpn-RM1 at concentration of 10³ copies/μl, and the PCR efficiency for each target was equivalent to DNA extracted from representative *S. pneumoniae* serotypes.

Conclusions: These modifiable and quantifiable multitarget plasmids simplify the preparation of controls for PCR-based serotyping of *S. pneumoniae*, allowing good quality control and standardization of PCR methods and reagents. While these plasmids were developed for pneumococcal disease surveillance, the rationale and design concepts could be extended to other highly multiplexed PCR assays.

2. ER STRESS MODULATES HERPES SIMPLEX VIRUS TYPE 1 (HSV-1) GENE EXPRESSION AND REPLICATION

Authors: M Thornbury, ES Pringle, BP Johnston, C McCormick

Affiliation: Department of Medicine, Microbiology and Immunology, Dalhousie University, Nova Scotia

Not published by request.

3. DISCOVERY OF A GENETIC SWITCH IN VIBRIO PARAHAEMOLYTICUS THAT CONTRIBUTES TO HOST CELL DEATH DURING INFECTION

Authors: L Getz, N Thomas

Affiliation: Dalhousie University, Department of Microbiology and Immunology, Halifax, Nova Scotia

Introduction: *Vibrio parahaemolyticus* (Vp) are human enteric pathogens that are the leading cause of seafood-borne gastroenteritis causing 5000 illnesses annually. Pandemic strains of Vp use, among other mechanisms, two Type 3 Secretion Systems (T3SS) to cause enteric and cytotoxic disease. The protein ExsA is vital in the activation of the cytotoxic T3SS. Currently, it is not fully understood how the *exsA* gene is activated and subsequently causes expression of the cytotoxic T3SS.

Methods: To discover a genetic switch that regulates *exsA* gene expression, we have designed a contemporary approach using a sensitive and responsive bioluminescence reporter. Mini-Tn5 mutagenesis was used to develop a 10,000-mutant library in a recombinantly engineered strain of Vp. This strain contains the LuxCDABE bioluminescent gene cassette transcriptionally fused to the *exsA* promoter. Subsequent screening of this library and the use of standard molecular genetics tools allowed us to identify transposon mutants with decreased ability to activate *exsA* gene expression. Secretion and cytotoxicity assays were used to characterize the virulence properties of these mutants.

Results: Screening of this library identified a gene encoding a putative DNA binding protein (YfgX). A YfgX mutant was significantly deficient in activating *exsA* gene expression. An in vitro Vp effector protein secretion assay revealed a deficiency in overall effector secretion for the YfgX mutant. Importantly, infection assays with the YfgX showed a significant decrease in host cell death.

Conclusions: YfgX encodes a putative DNA binding protein that is involved in activating *exsA* gene expression. The YfgX protein is required for efficient effector secretion and fulminant cell death during host infection. YfgX is an important regulatory protein whose function is vital for Vp virulence.

4. STOOL SPECIMENS THAT ARE TOXIC FOR CELL CULTURE SHOULD BE TESTED FOR CLOSTRIDIUM DIFFICILE CYTOTOXIN

Authors: AS Lang¹, L Mushanski¹, PN Levett¹

Affiliation: ¹Saskatchewan Disease Control Laboratory, Government of Saskatchewan Ministry of Health, Regina, Saskatchewan, Canada

Introduction: In 2016, 3853 stool specimens were submitted to the Saskatchewan Disease Control Laboratory (SDCL) for viral studies, 1679 for Clostridium difficile cytotoxin (CDT), and 752 for both. Samples cultured for viruses are sometimes toxic for cell culture and are reported to the physician as: “Due to specimen being toxic for cell culture, virus isolation cannot be performed”. This CPE is indistinguishable from that produced by CDT, so toxic viral studies samples were assessed for the presence of CDT.

Methods: Stool samples submitted to SDCL for viral studies that were toxic for cell culture were enrolled from May through December 2016. If there were no associated samples for CDT testing at SDCL, ordering physicians were contacted. If samples previously tested positive or negative, no further testing was carried out. If a previous testing was indeterminate or not carried out, the same sample submitted for viral studies was tested for CDT if the physician agreed.

Results: Thirty-nine samples submitted for viral studies at the SDCL were toxic for cell culture. Nineteen of 39 had previous or concurrent CDT testing, 16/39 were tested at the SDCL after consultation with the ordering physician, and 4/39 were lost to follow up. Of those samples that were previously tested, 14/19 were positive and 3/19 were negative for CDT; 2/19 were previously tested but results not divulged. Of the samples tested after consultation 13/16 were positive for CDT. Excluding samples with unknown previous results or those lost to follow up, 27/33 (81.8%) samples that were initially toxic for cell culture were positive for CDT.

Conclusions: The majority of specimens that were toxic for cell culture were positive for the presence of CDT. The report has been modified to include: “This result may be indicative of C. difficile toxin presence. Consider ordering C. difficile cytotoxin test on this sample if this test has not already been ordered.” This will help guide further testing and patient care.

5. PHYSICIAN AND PATIENT PERCEPTIONS OF HUMAN T-LYMPHOTROPIC VIRUS RISK IN SOLID ORGAN TRANSPLANTATION

Authors: G Patriquin^{1,2}, J Hatchette^{3,4}, TF Hatchette^{1,2}

Affiliation: ¹Department of Medicine, NSHA and Dalhousie University, Halifax, NS, ²Department of Pathology and Laboratory Medicine, NSHA, Halifax, NS, ³Research Services, IWK Health Centre, Halifax, NS, ⁴Department of Community Health and Epidemiology, Dalhousie University, Halifax, NS

Introduction: Human T-Lymphotropic Virus (HTLV) rarely results in disease, and has a low prevalence in Canada. Solid organs are screened for HTLV before transplantation, however the incidence of transplant-related HTLV disease is low even in the absence of screening. In this study, we assessed physician and patient knowledge, attitudes, and risk acceptance of HTLV in solid organ transplantation (SOT).

Methods: After piloting and ethics approval, physicians in Canadian academic institutions completed a web-based survey, and randomly-chosen local patients attending select clinics completed a questionnaire in person or by telephone. Surveys assessed knowledge of HTLV and, using standard gamble and time-trade-off methods, assessed theoretical risk of HTLV in SOTs.

Results: A total of 68 clinicians participated in the survey (response rate of approximately 14.8%). Approximately 26.1% of participants would recommend SOT regardless of community HTLV prevalence. In a community with prevalence resembling that of Canada, SOT recommendation rose to 45.8%. Only a minority of participating physicians would recommend against HTLV screening in Canada. Of 56 clinic patients, including 14 SOT recipients, approximately 11.5% would have rejected SOT regardless of HTLV risk, and 23.1% would have accepted SOT regardless of HTLV risk. When HTLV-related neurological sequelae were explained, the rejection rate increased to 26.9% and acceptance decreased to 19.2%. Recruitment is ongoing.

Conclusions: This is the first known study to address the opinions of HTLV risk by physicians and patients in Canada. Both groups were willing to accept some risk related to HTLV in SOT, however physicians would not abandon HTLV screening completely. This aligned with concerns implied by most patient respondents, especially regarding the potential for neurological disease.

6. INCREASING THE DIAGNOSTIC YIELD OF PNEUMOCOCCAL COMMUNITY ACQUIRED PNEUMONIA IN HOSPITALIZED ADULTS USING COMBINATIVE LABORATORY TESTING

Authors: A Oliver, M ElSherif¹, L Ye¹, D MacKinnon-Cameron¹, A Ambrose¹, M Warhuus¹, I Martin², TF Hatchette¹, S McNeil¹, J LeBlanc^{1*}, on behalf of the Serious Outcomes Surveillance (SOS) Network of the Canadian Immunization Research Network (CIRN)

Affiliation: ¹Canadian Center for Vaccinology (CCfV), IWK Health Centre, and Nova Scotia Health Authority (NSHA), Dalhousie University, Halifax, NS, Canada, ²Streptococcus and STI Unit, National Microbiology Laboratory, Public Health Agency of Canada, Winnipeg, MB, Canada

Introduction: The CIRN SOS Network has been performing active surveillance for pneumococcal community acquired pneumonia (CAP_{Spn}) in hospitalized adults since December 2010. This study evaluated the diagnostic yield for CAP_{Spn} of laboratory detection methods for *Streptococcus pneumoniae*, alone or in combination.

Methods: CAP was identified by chest radiography, clinical symptoms, and laboratory testing. *S. pneumoniae* isolates recovered from sputum and blood cultures were serotyped using the Quellung or PCR-based serotyping. Urine antigen detection (UAD) was also performed using a PCV13-serotype specific test (UADPCV13) or a commercial pan-pneumococcal UAD (UADSpn). Proportions for each test result (or combinations) were then divided into two serotypeable and non-serotypeable. The serotypeable results were further subdivided into proportion of 7- or 13-valent pneumococcal conjugate vaccine serotypes (PCV7 and PCV13, respectively), 23-valent pneumococcal polysaccharide vaccine serotypes (PPV23), or non-vaccine types (NVT).

Results: Of the 4769 all-cause CAP cases, 3110 (65.2%) had blood cultures, 1941 (40.7%) had a UADSpn, 1917 (40.2%) were tested using UADPCV13, and 1640 (34.3%) had a sputum culture. The proportion of *S. pneumoniae*-positive results for each individual test ranged from 7.1% to 10.3%. Using a combination testing, the diagnostic yield increased. Of the patients having received any of the detection tests for *S. pneumoniae* (n = 3705), 549 (14.8%) were identified as CAPSpn. For CAP cases who received all tests for pneumococci (blood and sputum culture, UADPCV13, and UADSpn), *S. pneumoniae* was identified in 23.2% (144/621). Similar trends were observed for serotypeable results (PCV7, PCV13, PPV23, and NVTs) and non-serotypeable results.

Conclusions: Overall, the contribution of *S. pneumoniae* to all-cause CAP in hospitalized adults was better defined using combination testing, as each tests increased the diagnostic yield.

7. IMPACT OF PRIOR SEASON VACCINATION ON SEASONAL INFLUENZA VACCINE EFFECTIVENESS: A PRELIMINARY ANALYSIS OVER 4 SEASONS FROM THE SERIOUS OUTCOMES SURVEILLANCE NETWORK OF THE CANADIAN IMMUNIZATION RESEARCH NETWORK

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Introduction: Recent controversy has arisen from observational studies suggesting a negative association between prior influenza vaccination and subsequent influenza vaccine effectiveness (VE). As immunologic theories suggest that impact of prior season vaccination could vary season to season, we investigated this association over 4 influenza seasons in Canada.

Methods: The CIRN SOS Network prospectively identified laboratory-confirmed influenza cases and influenza-negative controls admitted to participating hospitals. Using a test-negative control design, matched conditional logistic regression modeling stratifying participants into 4 groups (not vaccinated current or prior season [referent], vaccinated prior season only, vaccinated current season only, and vaccinated both current and prior season) was used to calculate odds ratios (OR) to estimate the effect of vaccination status on influenza-related hospitalization (VE= 1-OR x100). We assessed VE for overall effect and effect stratified by age (<65y, ≥65y), and strain (A/H3N2, A/H1N1, and influenza B) for 4 influenza seasons in Canada: 2011/2012-2014/2015.

Results: Although impact of prior vaccination varied, the largest effects were observed in H3N2 dominant seasons 2012/2013 and 2014/2015, seasons where the H3N2 vaccine component

was matched, and mismatched, respectively, to the circulating strain. In 2012/13, adjusted VE against influenza-related hospitalization was 62.5% (95% Confidence Interval [CI]: 41.5, 76.0%) for patients vaccinated in current season only, compared to 28.2% (9.9, 42.8%) among those vaccinated in both prior and current season. Restricting to only H3N2 hospitalizations in 2012/2013, VE was 58.6 (32.5-74.7) for current season only vaccinees, relative to 30.9% (10.8-36.5) in both seasons vaccinees. In 2014/2015, restricting to H3N2 hospitalizations yielded a similar trend: VE was 35.3% (95% CI: -32.6, 68.5%) in current season vaccinees compared to -8.3% (95% CI: -56.7, 25.1%) in both seasons vaccinees.

Conclusions: While our findings support a possible negative association between prior influenza vaccination and subsequent season VE for some seasons and strains, mainly non-statistically significant reductions in VE were observed. Future prospective studies, using varying methodology to examine this association and to explore contributing biological/immunological mechanisms, are critical to inform immunization policy.

8. TRANSLATION OF HERPESVIRUS MRNAS IS RESISTANT TO MTORC1 INHIBITION

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Not published by request.

9. DEVELOPMENT OF A SMALL ANIMAL MODEL TO TEST STRESS GRANULE-INDUCING ANTIVIRAL DRUGS

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Not published by request.

10. IDENTIFICATION AND CHARACTERIZATION OF REDOX PARTNERS OF THE THIOL-DISULFIDE OXIDOREDUCTASE SDBA IN STREPTOCOCCUS GORDONII

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Introduction: The formation of disulfide bonds by thiol-disulfide oxidoreductases (TDOR) is crucial for the proper folding and activity of many extracytoplasmic proteins. We recently identified a novel TDOR, SdbA, in *Streptococcus gordonii* that formed disulfide bonds in substrate proteins and played a role in multiple phenotypes. *S. gordonii* is a normal inhabitant of the human oral cavity and considered to be a pioneer colonizer of the tooth surface. It is also a candidate live oral vaccine vehicle.

Methods: Blast-search was used to find potential redox partners of SdbA. Mutants of the identified genes were created by an allelic replacement strategy. Mutants were analyzed for *sdbA* mutant associated phenotypes. Activity of redox partners was examined by disulfide exchange reactions.

Results: Four genes (*sdbB*, *ccdA2*, *sdbC*, and *ccdA1*) from two operons were identified as redox partners of SdbA from blast-search. The genes were systematically inactivated creating single- and double-gene mutants. The mutants were analyzed for *sdbA*-associated phenotypes. The results showed that inactivation of *sdbB* and *ccdA2* simultaneously, but not individually, replicated the *sdbA* mutant phenotype. In addition, AtIS, the natural substrate of SdbA, from the *sdbBccdA2* mutant lacked a disulfide bond and was inactive, indicating the primary redox partners of SdbA are SdbB and CcdA2. In disulfide exchange reactions, reduced SdbA was efficiently reoxidized by oxidized CcdA2 or SdbB. Interestingly, CcdA2 could also reoxidize SdbB suggesting that CcdA2 could serve as a redox partner of SdbA either directly or downstream of SdbB. In addition, two homologous proteins of SdbB and CcdA2, named SdbC and CcdA1, respectively, were identified as minor redox partners of SdbA.

Conclusions: *S. gordonii* has a very complex oxidative protein-folding pathway where SdbA-SdbB-CcdA2 constitutes the main pathway that affects autolysis, bacteriocin production, genetic competence, and eDNA release, while SdbA-SdbC-CcdA1 constitutes a minor pathway. The two pathways are interconnected with SdbB interacting with CcdA1 and SdbC with CcdA2.

11. A *SHIGELLA* EFFECTOR GOVERNS LYSOSOMAL EXPANSION

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Not published by request.

12. DISCRIMINATION OF VACCINE-PREVENTABLE STREPTOCOCCUS PNEUMONIAE SEROTYPES USING PCR AND SEQUENCING

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Introduction: Serotyping of *Streptococcus pneumoniae* is important to monitor disease epidemiology and assess the impact of pneumococcal vaccines. Traditionally, the Quellung reaction used serotype-specific antibodies to classify isolates based on differences in capsular antigens. More recently, PCR-based serotype deduction which have been broadly applied for pneumococcal surveillance, and relies on differences in the capsule biosynthesis genes (*cps* loci), and does not require live organism like Quellung serotyping. However, PCR lacks discrimination between certain serotypes. This study evaluated novel PCR and sequencing targets located inside the *cps* loci to discriminate vaccine-preventable serotypes of *S. pneumoniae*.

Methods: PCR and sequencing target were designed to detect and discriminate vaccine-preventable *S. pneumoniae* serotypes that could not be resolved using the CDC PCR-based serotyping method: 6A and 6B from 6C and 6D; 7F from 7A; 9V from 9A; 9N from 9L; 11A from 11D; 12F from 12A, 12B, 44 and 46; 15B from 15C; 18C from 18F, 18A, 18B; 22F from 22A, and 33F from 33A and 37. Specificity of each novel PCR and sequencing target was tested using: 1) the non-discriminated *S. pneumoniae* serotypes within the CDC PCR groups; 2) 90 different *S. pneumoniae* serotypes; and 3) 32 other streptococci. Reproducibility was evaluated using 10 to 20 replicates of each serotype, and represented geographically and genetically diverse strains.

Results: To date, all vaccine-preventable serotypes could be accurately discriminated using PCR and sequencing, and the results were highly reproducible among diverse *S. pneumoniae* isolates. No cross-reactions were observed between other *S. pneumoniae* serotypes or streptococci.

Conclusions: This study validated a novel molecular approach for accurately discrimination of vaccine-preventable serotypes of *S. pneumoniae*, which represents a significant technological advance for pneumococcal disease surveillance.

13. B1 CELL SUBSETS DIFFER BETWEEN THE SEXES AND ARE INVOLVED IN RESPONSES TO CHLAMYDIA INFECTION

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Introduction: *Chlamydia trachomatis* (*Ct*) is the leading cause of bacterial sexually transmitted infections worldwide. While the incidence of *Ct* in females is persistently higher than males, it is unclear whether this is related to sex-specific differences in the immune response to infection. This study focuses on sex-specific differences in innate-like B cells (ILBs), specifically B1 cells. It has been demonstrated that ILBs play a role in *Chlamydia* infection but ILBs have never been examined in the context of sex-specific immune responses to *Chlamydia*.

Methods: Mice were infected intranasally with a mouse model of *Chlamydia*, *C. muridarum* (*Cm*), to examine if immune responses to *Cm* differed between the sexes. Cells were isolated from the lung and draining lymph node (DLN) and analyzed by flow cytometry, while bacterial burden was measured using qPCR. In a separate experiment, cells were isolated from naive mice to investigate the possibility of sex-specific differences in B1 cell populations at rest. Finally, various B cell subsets were co-cultured with T cells and stimulated with heat-killed *Cm*. The supernatant from this co-culture was collected and analyzed by cytokine ELISA to identify the type of T cell response supported by various B cell subsets.

Results: In the intranasal infection model, females lost more body weight compared to males despite comparable bacterial burden. Compared to males, females also had significantly higher numbers of follicular T helper cells, follicular B cells, and B1 cells in the DLN. In naive mice, B1 cell distribution in a variety of sites in male and female had differential distributions, with CD5+ B1a and CD5- B1b cells having a higher proportion of the B1 population in female and male mice, respectively. Subsequent co-culture experiments suggested that B1a cells promoted IL-10 production while B1b cells stimulated IFN- γ production in response to *Chlamydia* infection.

Conclusions: Taken together, our data demonstrates that B1 cells differ between the sexes and are actively involved in the immune response to *Chlamydia* infection.

14. INFLUENZA VACCINE EFFECTIVENESS IN THE PREVENTION OF INFLUENZA-RELATED HOSPITALIZATION IN CANADIAN ADULTS OVER THE 2011/12 THROUGH 2013/14 SEASON: A POOLED ANALYSIS FROM THE SERIOUS OUTCOMES SURVEILLANCE (SOS) NETWORK OF THE CANADIAN INFLUENZA RESEARCH NETWORK (CIRN)

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Introduction: Ongoing assessment of influenza vaccine effectiveness (VE) is critical to inform public health decision making. The CIRN SOS Network provides annual estimates of influenza VE in the prevention of influenza-associated hospitalization in adults. Here we provide pooled VE estimates across three influenza seasons.

Methods: From 2011/12-2013/14, the SOS Network conducted active surveillance for influenza among hospitalized adults ~1 Nov – 30 April in up to 45 hospitals in 7 provinces. A nasopharyngeal swab for influenza polymerase chain reaction (PCR) was obtained from all patients admitted with any acute respiratory diagnosis or symptom. Cases were PCR-positive

for influenza; test-negative controls were enrolled and matched for date, enrolment site and age of the case ($\geq 65y$ vs. $< 65y$). VE was estimated as $(1 - OR \text{ of influenza in vaccinated vs. unvaccinated patients}) \times 100$ for cases and controls enrolled over 3 seasons. VE estimates were adjusted using multivariable logistic regression with stepwise backward selection of covariates with p-value of $< .1$ in univariate analysis.

Results: 3394 cases and 4560 controls were enrolled; 2078 (61.2%) cases and 2939 (64.5%) controls were $\geq 65y$. Over 3 seasons, overall matched, adjusted VE was 41.7% (95% Confidence Interval [CI]: 34.3, 48.3%); corresponding VE in adults $\geq 65y$ was 39.3% (95% CI: 29.4, 47.8%) and in adults 16-64y was 48.0% (95% CI: 37.5-56.7%). Including all age groups, VE against influenza A was 44.1% (95% CI: 35.1, 51.9%) and against influenza B was 35.3% (95% CI: 20.7, 47.3%). In adults $\geq 65y$, VE against influenza A/H3N2 and A/H1N1 was 24.2% (95% CI: 3.6, 40.4) and 58.7% (95% CI: 39.4, 71.9%), respectively. Corresponding estimates in 16-64y were 44.4% (95% CI: 19.0, 61.8%) & 60.8% (95% CI: 45.1, 72%), respectively.

Conclusions: While effectiveness of influenza vaccines to prevent serious outcomes varies year to year due to factors such as virulence and match between circulating and vaccine strains, we demonstrate statistically and clinically important benefit of vaccination in adults over three seasons, with an average overall effectiveness of 42%.

15. VACCINE EFFECTIVENESS (VE) OF NON-ADJUVANTED AND ADJUVANTED TRIVALENT INACTIVATED INFLUENZA VACCINES (TIV) IN THE PREVENTION OF INFLUENZA-RELATED HOSPITALIZATION IN CANADIAN SENIORS OVER THE 2011/12 THROUGH 2013/14 SEASON: A POOLED ANALYSIS FROM THE SERIOUS OUTCOMES SURVEILLANCE (SOS) NETWORK OF THE CANADIAN IMMUNIZATION RESEARCH NETWORK (CIRN)

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Introduction: Influenza vaccines represent our best tool for preventing influenza-related morbidity and mortality in Canadian adults. However, vaccine effectiveness (VE) of trivalent influenza vaccine (TIV) in seniors (≥ 65 y) is suboptimal. An MF-59 adjuvanted TIV ($_{\text{adj}}$ TIV) developed to improve VE in seniors was authorized in Canada for patients ≥ 65 y beginning in the 2011/12 season. Here we pool three influenza seasons (2011-2014) to estimate the VE of $_{\text{adj}}$ TIV and non-adjuvanted TIV ($_{\text{n-adj}}$ TIV) for the prevention of influenza-associated hospitalizations in Canada.

Methods: The SOS Network conducted active surveillance for influenza among hospitalized adults from 2011/12 - 2013/14 in up to 45 hospitals in 7 provinces. Using the test-negative control design, influenza-positive cases and matched influenza-negative controls who were vaccinated with $_{adj}$ TIV or with $_{n-adj}$ TIV and who were ≥ 65 years old were identified. Odds ratios for influenza were calculated using multivariable logistic regression with backwards stepwise for important confounders such as age, receipt of antivirals, frailty, smoking history and medications. VE was then calculated using $(1-OR) \times 100\%$ with accompanying 95% confidence intervals (CIs).

Results: In all patients ≥ 65 y in the three pooled seasons, 284 patients received $_{adj}$ TIV (Fluad[®]) and 2049 received $_{n-adj}$ TIV. Patients who received $_{adj}$ TIV were older than $_{n-adj}$ TIV patients (mean age: 83.5 vs 79.8, $p < 0.001$), and were more likely to be admitted from a long-term care facility (57.3% vs 5.6%, $p < 0.001$). A higher proportion of $_{adj}$ TIV patients were also in the highest category of frailty prior to admission (19.7% vs 2.6% in $_{n-adj}$ TIV patients, $p < 0.001$). Overall, in patients ≥ 65 y, adjusted VE of $_{adj}$ TIV (n= 286 cases/327 controls) was 61.3% (95% CI: 17.5, 81.9%) and adjusted VE of $_{n-adj}$ TIV (n=1038 cases/1304 controls) was 32.5% (95% CI: 18.9, 43.7%).

Conclusions: These findings indicate a trend that $_{adj}$ TIV may be providing better protection against influenza-associated hospitalizations in seniors than $_{n-adj}$ TIV products currently used in Canada, particularly given that a high proportion of the $_{adj}$ TIV group were frail, elderly patients who usually see minimal benefit from influenza vaccination.

16. EVALUATION OF THE ZEUS ELISA™ *BORRELIA* VISE1/PEPC10 IGG/IGM ENZYME IMMUNOASSAY (EIA) FOR SEROLOGICAL DETECTION OF LYME DISEASE

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Introduction: Currently, the serological diagnosis of *Borrelia burgdorferi* infection in Canada is based on the two step algorithm recommended by the the Centers for Disease Control (CDC) consisting of an enzyme immunoassay (EIA) followed by IgM/IgG immunoblots (IB). This study evaluated the ZEUS ELISA *Borrelia* VIsE1/pepC10 IgG/IgM EIA compared to the whole cell (WC) lysate EIA (ZEUS ELISA *B.burgdorferi* IgG/IgM) and the C6 EIA (Immunitics) in the two step algorithm for serological diagnosis of *B. burgdorferi* infection.

Methods: 90 residual sera previously submitted for Lyme disease serology (includes IB + and - specimens) and 60 specimens from healthy controls were tested by each of the three EIAs. Specimens positive or equivocal by EIA were tested at the NML by IB and scored according to the CDC criteria. In addition, the NML uses "borderline" (BL) categories for sera where 4/10 CDC bands on the IgG are reactive, with a weakly reactive fifth band or the VIsE band present; for the IgM only the p25 band is reactive.

Results: Overall 66/90 (49 positive; 11 negative) results were concordant between all three EIAs. Eleven specimens were positive only by the WC EIA. The VIsE1/pepC10 EIA identified 11 specimens that were not detected by the C6 EIA (WIB - = 5; IgM IB +/- IgG IB - = 3; IgG IB + = 3). In our specificity panel, 10% of specimens (6/60) were positive on the VIsE1/pepC10 EIA; all were negative on IgG IB; 2 were BL by IgM IB.

Conclusions: The VIsE1/pepC10 EIA identified 11 sera not detected using the C6 EIA; these were positive (n=4) or BL (n=3) by IgG IB suggesting that it is more sensitive than the C6 EIA. Without clinical data, it is not possible to determine if positive EIA results in the specimens with negative IBs were due to detection of early serologic response in acute localized infection or false positive EIA results. The specificity of the VIsE1/pepC10 EIA was 90% and this supports the need to continue supplemental testing with IBs.

17. ENHANCING DETECTION AND RESPONSE FOR FUTURE INTERVENTIONS: BUILDING SUSTAINABLE COMMUNITY-BASED CAPACITY THROUGH THE EXPERIENCES OF MOBILE LAB AND CLINICAL TRIAL INTERVENTIONS

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Introduction: Scarce knowledge exists on how Ebola virus disease (EVD) interventions were received by communities and local community health workers in West Africa. Strengthening health systems and enhancing global ability to detect and respond to future outbreaks and health emergencies requires understanding such social dynamics. This study focuses on medical interventions during the Ebola crisis which continue to challenge effective immunization and public health strategies. We present initial analyses that are contributing to the development of an evidence-based, contextually-sensitive and flexible decision-making framework for use by national health authorities in low income countries to prioritize health interventions and strengthen community health surveillance and response.

Methods: Qualitative interviews were conducted with survivors, local, national, and international scientific, health, and policy responders to the West African Ebola epidemic through the multi-country, multi-institutional Ebola 100 (www.ebola100project.net) and Institut Pasteur Study on Biomedical Engagement in the West African Ebola epidemic Archive Project. This translational research focuses on the interactions between a diverse range of rationales and practices (logics) of global, national and local communities surrounding critical interventions that will be used to develop an analytical decision-making framework to aid future interventions.

Results: We present responders' experiences with the local, national, and international acceptance of emergency interventions including EVD testing, triage, isolation, and medical treatment emergency interventions, and examine how these aligned with local, national, and international scientific, global health, and political priorities between West African governments and societies and wealthy donor countries.

Conclusions: This research offers insights into the intersection between public policy during global health emergencies and the translation of filovirus research and clinical science into practice. Grounded in the perspectives of anthropology, science studies, technology assessment and humanitarian practice, and in conjunction with clinical science, this framework features knowledge that reflects local contextual needs, regional priorities, and scientific

capabilities and limitations. The framework situates community surveillance at the centre of effective response to infectious disease outbreaks.

18. KEEPING MOM AND BABY HEALTHY- AN IMMUNIZATION PILOT PROJECT

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Introduction: Vaccinating pregnant women against influenza and pertussis has been shown to protect the pregnant woman, the fetus in-utero and the newborn, however, immunization rates in pregnancy remain low. Our outpatient Perinatal Centre has identified the need to improve immunization rates, however current staffing levels are not able to facilitate this. Patients are therefore referred to their family physician or community pharmacists for immunizations. The literature however, has shown that immunization coverage is improved when the vaccine is provided at the time of recommendation, as opposed to when a person is referred to another provider.

Methods: Pharmacists in our province have been permitted to provide immunizations since 2013. A pharmacist with certification to administer vaccines was integrated into the Perinatal Centre to screen clinic attendees for required immunizations, prescribe and to administer vaccines when appropriate. The pharmacist spent 7 days in the Perinatal Centre over a 1 month period. Nurses and physicians were educated regarding the recommendations for vaccinations in pregnancy. A “Vaccinations for Pregnant Women” patient pamphlet and a “Perinatal Care Immunization Orders” form were created. Also, our institution’s immunization policy was updated to include pharmacists.

Results: The pharmacist assessed patients, provided counseling and prescribed and administered 81 vaccinations to pregnant women over the 7 day trial period. While onsite, the pharmacist was also able to answer drug information questions, identify and resolve any drug therapy problems and provide medication reviews to other pregnant patients in the Perinatal Centre.

Conclusions: As a result of the positive feedback from the pilot, a pharmacy consult service is under development for the Perinatal Centre. Clinical pharmacists will be able to be consulted to see high risk outpatients, provide immunizations, provide medication reviews, or provide education to patients and team members on the safety of medications in pregnancy and breastfeeding.

19. A SYSTEMATIC REVIEW OF ANTIMICROBIAL STEWARDSHIP INTERVENTIONS IN THE EMERGENCY DEPARTMENT

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Introduction: Infections are one of the most frequent reasons patients present to the emergency department (ED), often resulting in antimicrobial prescribing. Implementation of antimicrobial stewardship programs in the ED has been recommended to improve antimicrobial utilization in this setting. The primary objective of this study was to characterize antimicrobial stewardship (AMS) in the ED and to identify interventions that improve patient outcomes and/or reduce consequences of antimicrobial use.

Methods: A systematic review was completed to meet study objectives. Medline, EMBASE, Cumulative Index to Nursing and Allied Health Literature, Scopus, and Web of Science were searched from inception through November 2016. All randomized controlled trials, non-randomized controlled trials, controlled and uncontrolled before-after studies, interrupted time series studies, and repeated measures studies which evaluated AMS interventions and reported on patient outcomes, quality of care, or utilization of antimicrobial agents were included in the review. Studies published in languages other than English were excluded.

Results: Forty-three studies met inclusion criteria. Most studies were uncontrolled before and after studies with unclear or high risk of bias. The most frequently reported interventions were patient or provider education and guideline or clinical pathway implementation alone or in combination with other interventions. Only 6 studies reported on prescriber audit and feedback. Mixed findings on impact of interventions were identified. Benefits of AMS interventions often included improvement in delivery of care or a decrease in antimicrobial utilization.

Conclusions: Implementation of AMS in the ED has the potential to improve patient care however; the majority of studies evaluating antimicrobial stewardship in the ED lacked rigorous design. In addition, few studies evaluated recommended core components of AMS programs including prescriber audit and feedback and pre-authorization. Further high quality research is needed to identify the exact interventions, or combination of interventions, which will optimize antimicrobial use in this setting.

20. THE INCIDENCE OF COMMUNITY ACQUIRED PNEUMONIA BY OCCUPATION

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Introduction: Reversible, modifiable risk factors are associated with a greater risk of developing community acquired pneumonia (CAP). Many studies have linked exposure to welding fume to a greater risk of developing pneumococcal pneumonia and invasive pneumococcal disease as well as dying from the disease. Welders of working age are 3.5 times more likely to die from pneumococcal pneumonia than men in other jobs. A higher risk of CAP is seen in workers exposed to any type of metal fume and this excess risk is limited to men below the normal retirement age of 65 years, indicating that susceptibility to pneumonia is reversible. Often it is not the occupation of the individual but recent working conditions that are related to the development of CAP.

Methods: At 12 sites across Canada patients who have been admitted to hospital with CAP have been recruited to participate in the CAP/IPD study. As a pilot study questions regarding occupation were asked in 4 sites. The information was then coded using the Canadian National Occupational Classification (NOC) 2011. These data were used to calculate percentages and compare occurrences of pneumonia across occupations.

Results: We obtained occupation data on 171 cases. The NOC codes were analysed by aggregating data to the ten single digit NOC codes. Those involved in “trades, transport and equipment operators and related fields” comprised 26% (n=44) of cases when including retired workers. There was a significantly greater proportion of cases 32% (n=29, p = 0.05, Chi = 3.834) amongst current workers in “trades and related occupations” compared to workers in all other jobs 68% (n=62). There were five single digit NOC codes including “trades and related occupations” where the proportion of cases amongst current workers was higher than in those retired.

Conclusions: Our data suggests that workers in “trades and related occupations” are more at risk of CAP with the proportion affected exceeding that of those employed in this group, 25.5 % (Statcan, 2011). Although various studies have examined the impact of occupational exposure on the respiratory system few have analyzed occupations and exposure as risk factors for developing CAP. The reduced proportion of cases in those retired from “trades and related occupations” compared to current workers may represent an occupational effect.

21. DECLINE IN HOSPITALIZATION DUE TO PNEUMOCOCCAL AND ALL-CAUSE PNEUMONIA IN CANADIAN CHILDREN, 2004 TO 2015

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Introduction: Pneumonia is a common, potentially severe illness that results in the hospitalization of over 7000 children in Canada every year. Pneumococcal conjugate vaccine (PCV) was introduced in Canada in 2002, and public health programs were funded by all provinces by 2006. This led to the decline in the incidence of invasive pneumococcal disease (IPD); however, the emergence of non-vaccine serotypes eroded some of these gains. The introduction of PCV10 in 2009 in some provinces and PCV13 in all provinces by 2011 resulted in the further decline of IPD, but information is needed on the effect of these programs on pneumococcal pneumonia (PP) and all-cause pneumonia (ACP). This retrospective study was undertaken to determine pediatric hospitalization rates of PP and ACP in Canada (excluding Quebec, and BC after 2010) from 2004 to 2015.

Methods: Case data were obtained from the Canadian Institute for Health Information Discharge Abstract Database, which contains data on hospital discharges across Canada, derived from patient administrative and clinical record systems. PP and ACP were defined using the ICD-10-CA codes. Data are included from all Canadian provinces except Quebec, which employed ICD 9th Revision codes for part of the study period, and excluding BC after 2010 due to unavailability of data. Population data were obtained from Statistics Canada.

Results: The incidence of hospitalized PP in children <5 years declined from 10.6 per 100,000 per year in 2004/05 to 7.1 in 2005/06, but then increased to 9.15 in 2010/11, coinciding with the emergence of non-vaccine serotypes. After the introduction of higher valence PCVs the rate then declined to its lowest rate of 2.88 in 2013/14. Similarly, the incidence of ACP declined from 693 (per 100,000 per year) in 2004/05 to 535 in 2007/08, then increased to 921 in 2010/11. This was followed by a decline to its lowest rate of 452 in 2013/14. A rebound to 503 was observed in 2014/15.

Conclusions: The temporal trends in the incidence of hospitalized ACP in children < 5 years paralleled that of PP from 2004/05 to 2014/15. The decline of PP by 2013/14 was 7.72 per 100,000 per year (73%), while the decline of ACP over the same time period was 241 (35%). Although more investigations are needed to understand this relationship, the impact of PCV on the disease burden may be greater than estimated by PP alone.

22. CUMULATIVE IMMUNE FUNCTION BEFORE AND AFTER HCV DIRECT-ACTING ANTIVIRAL CURE

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Introduction: Assessing the quality of immune responses in HCV-infected individuals who achieve treatment-based viral cure is a high priority. However, studies often focus on one aspect of the immune system as opposed to considering cumulative immune function as a whole on a per-individual basis. This limits our ability to understand and predict what constitutes an effective immune response in HCV⁺ people on direct-acting antiviral (DAA) cure. We determine immune cell phenotype and function in individuals with chronic HCV infection before and after HCV DAA-induced viral cure, and assess overall immunity per individual.

Methods: HCV subjects were treated with DAA regimens for 12 weeks. Comprehensive T cell, B cell, and NK cell immunophenotyping was performed on peripheral blood cells from these individuals, as well as age and sex matched controls, at baseline, end of treatment (EOT), and post-treatment follow-up week 24. Polychromatic flow cytometry, in vitro enzyme-linked immunospot (ELISPOT), and cytotoxicity assays simultaneously assess phenotype and function in T cell subsets, B cells, and NK cells.

Results: All individuals had HCV viral suppression on DAA therapy. Markers of T cell immune exhaustion, including PD-1, Tim-3, and CTLA-4 decrease with viral suppression. The frequency of inhibitory receptor⁺ NK cells changed with therapy within an individual and across the study population. NK cells from some individuals has augmented cytotoxicity with viral suppression compared to before treatment. In contrast, abnormal frequencies of multiple B cell subpopulations at baseline persisted despite viral suppression. HCV-specific T cell responses were more frequent at EOT compared to those at baseline.

Conclusions: Immune phenotypes become less senescent overall with viral suppression, however residual deficits remain. When assessed cumulatively, immune senescence improves with viral suppression, in terms of both HCV-specific, as well as bystander immune cell exhaustion. This may have implications for HCV vaccine strategies, as well as personalized approaches to HCV therapy.

23. IMMUNOSENESCENCE PHENOTYPES ARE IMPACTED BY HCV NS5A INHIBITION MORE THAN NS5B OR NS3 INHIBITION

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Introduction: Treatment of chronic HCV infection with a direct-acting antiviral (DAA) combination containing an NS5B inhibitor and the immune modulating antiviral ribavirin is associated with restoration of immune cell function. Evidence suggests that HCV proteins, such as NS5A, have direct immune modulatory function that contributes to viral persistence. It is important to understand if inhibition of targets such as NS5A enhance immunity and potentially facilitate shorter HCV treatments. We assess the effect of HCV polymerase (NS5B), protease (NS3), and NS5A inhibitors on in vitro immune cell phenotypes.

Methods: Peripheral blood mononuclear cell (PBMC)-derived T cell and NK cell phenotypes from HCV-infected and uninfected individuals were evaluated by flow cytometry at baseline and after 7 days in the absence or presence of individual DAAs in vitro. PBMC and Huh-7.5 cells infected with the Cp7 J6/JFH1 HCV strain were cultured across a transwell with inhibitors for NS5B (sofosbuvir), NS3 (GS-9451), NS5A (ledipasvir), or vehicle control. Total cell numbers and viability were assessed on days 3, 5, and 7.

Results: DAA exposure in the absence of HCV production by Huh-7.5 cells did not impact expression of immune markers, and did not significantly affect cell growth or viability. At baseline, T cells expressing markers of immune exhaustion, including PD-1, CTLA-4, and Tim-3, were more frequent in PBMC from chronically infected HCV treatment-naïve individuals compared to those from uninfected individuals. NS5A inhibition led to reduced frequency of PD-1⁺ T cells, whereas neither NS5B nor NS3 inhibitor altered immune exhaustion marker expression after 7 days. There were no significant differences in NK cell phenotype between the drugs tested or vehicle alone.

Conclusions: NS5A inhibition decreases immune exhaustion markers after only 7 days. These data suggest that an NS5A inhibitor may be an important immune enhancer above and beyond viral inhibition. In shortened regimens, or individuals who are difficult to treat, maintaining NS5A inhibition and enhancing host response may be an important part of the antiviral strategy.

24. A COMPARISON OF VARIOUS MEDIA FOR THE GROWTH OF CARBAPENEMASE-PRODUCING ORGANISMS

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Introduction: Screening for carbapenem-producing organisms using stool samples is complicated by the multiple species of carbapenem-resistant *Enterobacteriaceae* (CRE) and enzymes that occur. We assessed screening media to determine which would enable detection with minimal workload.

Methods: We compared the cost, sensitivity and specificity of a MacConkey medium containing 0.2 mg/L meropenem (Mero-Mac) and three commercial chromogenic media: Alere SuperCarba, Biomerieux CarbaSmart Carb/OXA bi-plate, and Fisher Chromogenic ESBL (extended-spectrum β -lactamase)/CRE bi-plate. A 5 % sheep blood agar (SBA) was used as a non-selective media. A 0.5 McFarland suspension of a culture grown on SBA was serially diluted with no pre-enrichment. Four dilutions (log 6 to log 3 cfu/ml) of each organism were compared. A 32-pin replicator tool was used to deliver ~8 ul bacterial suspension to the surface of the agar. The experiment was performed in duplicate. The isolates included: 35 CREs (10xKPC, 8xSME, 4xVIM, 4xNDM, 3xOXA-48, 1 each of OXA-48/NDM, GES-5, IMP, NMC, OXA-23, OXA-24), some of which contained additional β -lactamases. Non-carbapenemase isolates were as follows: 24 with one or more β -lactamases such as AmpC or ESBL and 21 with no genes detected by PCR. The growth and color of the colonies was recorded at 18-24 h and 48 h (recommended by the manufacturers). We calculated the sensitivities and specificities for growth of each isolate at each dilution, and the utility of colony color. The lowest limit of detection was recorded for each isolate.

Results: The Mero-Mac was inexpensive, had 100% sensitivity to all CPOs but a specificity of 37%. The CarbaSmart Carb media had high sensitivity (96%) and specificity (97%) but using the manufacturer's colony color guideline reduced the sensitivity (77% at 24 h; 83% at 48 h). The Chromogenic ESBL and CRE media failed to detect SME and NMC and one KPC, resulting in low sensitivities (69% and 71%). Their specificities were 33% and 56%, and the results did not change significantly when color was assessed. The SuperCarba detected some SME, and had a sensitivity of 83% and specificity of 61%. The CarbaSmart OXA media performed well for three of four OXA-48, and had high specificity (99%).

Conclusions: The Mero-Mac medium was highly sensitive, the least expensive, but lacked specificity. The CarbaSmart Carb medium had higher sensitivity and specificity than the other chromogenic media. Other chromogenic media failed to detect particular types of CPOs (SME, NMC). The chromogenic speciation of bacteria and OXA-48 identification was of limited value

in screening. Reading the plates at 24 h could improve the specificity and turnaround time while only slightly decreasing the sensitivity for some plates.

25. INFLUENZA BURDEN, RISK FACTORS FOR SEVERE DISEASE AND INFLUENZA VACCINE EFFECTIVENESS AMONG PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) ADMITTED TO HOSPITAL WITH LABORATORY-CONFIRMED INFLUENZA: A STUDY FROM THE SERIOUS OUTCOMES SURVEILLANCE (SOS) NETWORK OF THE CANADIAN IMMUNIZATION RESEARCH NETWORK (CIRN)

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Introduction: International guidelines recommend annual influenza vaccination for patients with COPD to reduce exacerbations, however vaccination uptake remains suboptimal. To enhance our understanding of influenza burden and morbidity, we examined risk factors for serious influenza outcomes in hospitalized adults with COPD, and assessed influenza vaccine effectiveness (VE) in preventing hospitalization.

Methods: We conducted a post-hoc analysis of national, prospective, multi-center, cohort data. We included hospitalized adults with COPD and PCR-confirmed influenza admitted during four consecutive influenza seasons (2011- 2015). We determined risk factors for death and intensive care unit (ICU) admission, and calculated VE against influenza-associated hospitalization using a test-negative design in a separate cohort of influenza cases and test-negative controls. Crude VE estimates were adjusted using multivariable logistic regression.

Results: Among 1847 hospitalized patients with COPD and PCR-confirmed influenza, 18.1% (n=335) were admitted to ICU, 9.6% (n=177) required mechanical ventilation, and 11.2% (n=206) died within 30 days after hospital admission. Among patients with known vaccination status, 59% (887/1504) received influenza vaccine. Significant risk factors for death included comorbid cardiac disease (OR 2.0; 95% CI 1.3-3.1), admission from long-term-care (OR 2.7; 95% CI 1.6-4.6), and home oxygen use (OR 2.8; 95% CI 1.6-5.0). Risks for ICU admission included comorbid diabetes (OR 1.6; 95% CI 1.2-2.2), current smoking (OR 2.0; 95%CI 1.5-2.7), and home oxygen use (OR 1.9; 95% CI 1.2-2.9). Overall adjusted VE for the prevention of influenza-associated hospitalization in patients with COPD was 41.5% (95% CI 29.0% - 51.8%).

Conclusions: Despite guideline recommendations, only 59% of hospitalized patients with COPD and influenza received influenza vaccine. The estimated VE suggests that increasing influenza vaccination rates in COPD patients could significantly reduce hospitalization rates and subsequent health care costs.

26. INFLUENZA VACCINE RESPONSES ARE LIMITED IN HIV POSITIVE INDIVIDUALS, AND NOT PREDICTED BY ALTERED B CELL PHENOTYPE

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Introduction: Human Immunodeficiency Virus (HIV) is a chronic disease, and while antiretroviral (ARV) agents allow for disease control, long lasting immune changes persist. Influenza vaccination is recommended for HIV⁺ patients even though it is known that it is less effective in providing immunity. It is not clear if there are clinical or immune cell markers that are predictive of influenza vaccine response in HIV⁺ individuals. This study aimed to identify immune cell exhaustion and clinical markers associated with poor response to influenza vaccination in HIV⁺ patients.

Methods: Peripheral blood mononuclear cells (PBMC) from 12 HIV⁺ patients (10 male, 2 female) were collected pre-influenza vaccination and 6 months post vaccination after obtaining informed consent. Hemagglutinin Inhibition assays for the 3 components of the 2015-2016 trivalent influenza vaccine were performed. Standard of care clinical and virologic data were obtained through routine blood draws. B cell (CD10, CD19, CD20, CD21, CD27) and T cell (CD3, CD4, CD8, CD27, CD28, Tim-3, PD-1, CTLA-4, and CD57) immunophenotyping was performed. CMV status was determined by clinical and in-house serologic assay, as well as T cell ELISpot.

Results: Influenza vaccine titers were low or limited, with only 5 influenza responders regardless of previous vaccination, and no self-reported influenza disease. Influenza response was not predicted by CD4⁺ T cell count, CD4:CD8 ratio, viral load suppression or the frequency of B cell tissue like memory (TLM) cells. TLM B cells were not elevated in the responders versus non-responders. CMV responses were present in the all individuals, and data on the correlation between influenza titer, and CMV specific T cell responses will be presented.

Conclusions: Poor responsiveness to a potent vaccine such as influenza is not directly related to traditional immune exhaustion markers. A more comprehensive analysis of cumulative immunity will be necessary to accurately predict vaccine response.

27. IMPACT OF CONJUGATE VACCINES ON INVASIVE HAEMOPHILUS INFLUENZAE TYPE B (HIB) AND STREPTOCOCCUS PNEUMONIAE INFECTIONS IN CHILDREN WITH CANCER: A REPORT FROM THE CANADIAN IMMUNIZATION MONITORING PROGRAM ACTIVE (IMPACT)

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Introduction: Children undergoing cancer treatment are at increased risk of invasive *Haemophilus influenzae* type b (Hib) and invasive pneumococcal disease (IPD). The epidemiology of these diseases in children with cancer has not been described in the post-Hib vaccine and pneumococcal conjugate vaccine (PCV) era. The Canadian Immunization Monitoring Program Active (IMPACT) conducts active surveillance for Hib and IPD at 12 pediatric tertiary care centres. Our objective was to describe clinical features and outcomes of invasive Hib and IPD among children with cancer reported to IMPACT from 1991 to 2014.

Methods: We analyzed IMPACT reports of invasive Hib and IPD among children with cancer 0–16 years of age who were receiving cancer treatment or post-hematopoietic stem cell transplant (1991–2014). Demographic and clinical data were extracted from IMPACT databases for analysis.

Results: Thirteen cases of invasive Hib and 303 cases of IPD were reported among children with cancer. Age distribution of invasive Hib cases was: 4 (31%) 2–4 years of age, and 9 (69%) ≥5 years of age. Age distribution of IPD cases was: 22/303 (7%) <2 years of age, 115 (38%) 2–4 years, 153 (50%) ≥5 years of age. Six patients with Hib (46%) were age-appropriately. Among patients presenting after PCV licensure (2001), 29/169 (17%) were age-appropriately. 7% of Hib and 20% of IPD cases had unknown vaccination history. Bacteremia was the most common presentation of Hib and IPD (54% and 67%, respectively). ICU admission was required in 23% of Hib and 8% of IPD cases. One child died of Hib and 4 died of IPD.

Conclusions: Invasive Hib and IPD occurred predominantly in children with cancer ≥5 years of age and were associated with morbidity and mortality. Results suggest that less than 50% of patients were fully immunized for age. The findings suggest a need for further research into the effectiveness of Hib and PCV immunization in this high-risk population to optimize immunization strategies.

28. VALIDATION OF PCR-BASED DETECTION AND SEROTYPE DEDUCTION OF STREPTOCOCCUS PNEUMONIAE FROM NASOPHARYNGEAL SWABS COLLECTED FOR VIRAL STUDIES IN CASES OF COMMUNITY-ACQUIRED PNEUMONIA

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Introduction: Detection and serotyping of *Streptococcus pneumoniae* is important to assess the impact of pneumococcal vaccines. This study describes the diagnostic accuracy of PCR-based detection of *S. pneumoniae* directly from nasopharyngeal (NP) swabs collected for respiratory virus studies.

Methods: Active surveillance for community acquired pneumonia (CAP) in hospitalized adults was performed from December 2010 to 2013. Detection of pneumococcal CAP (CAP_{Spn}) was performed by urine antigen detection (UAD), identification of *S. pneumoniae* in sputum or blood cultures. *S. pneumoniae* was detected in NP swabs using *lytA* and *cpsA* real-time PCR, and serotyping was performed using conventional and real-time multiplex PCRs. For serotyping, the Quellung reaction, PCR-based serotyping, or a serotype-specific UAD was used.

Results: NP swab results were compared against CAP cases where all pneumococcal tests were performed (n = 434), or where at least one test was performed (n = 1616). CAP_{Spn} was identified in 22.1% (96/434) and 14.9% (240/1616), respectively. The sensitivity of NP swab PCR for the detection of *S. pneumoniae* was poor for CAP_{Spn} [35.4% (34/96) and 34.17% (82/240)], but high specificity was observed [99.4% (336/338) and 97.89% (1347/1376)]. Of the positive NP swabs, a serotype could be deduced by PCR in 88.2% (30/34) and 93.9% (77/82), respectively.

Conclusions: While further optimization may be needed to increase the sensitivity of PCR-based detection and serotyping, its high specificity suggests there is value for pneumococcal surveillance. With many laboratories archiving specimens for influenza virus surveillance, this specimen type could provide a non-culture based method for pneumococcal surveillance.

29. ACTIVATION OF LXRA INHIBITS KAPOSI'S SARCOMA-ASSOCIATED HERPESVIRUS
REPLICATION

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Not published by request.

30. ANTIMICROBIAL POINT PREVALENCE SURVEY IN NOVA SCOTIA ACUTE CARE HOSPITALS

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Introduction: Point prevalence surveys (PPS) are used to monitor antimicrobial use and identify targets for improvement through antimicrobial stewardship activities. The objective of this study was to determine the point prevalence and characterize antimicrobial use in Nova Scotia hospitals.

Methods: A PPS was conducted on all patients admitted to pediatric and adult hospitals with at least 30 acute care beds between June and September 2015. The primary outcome was the number of patients who received a systemic antimicrobial agent by 8:00 a.m. on the day of the survey divided by the total number of patients admitted to each ward. Secondary outcomes included the type of antimicrobial agent prescribed, dose, route of administration, intended duration of use, and indication. Adherence to treatment guidelines developed in 2012 by the adult tertiary hospital, and available to all prescribers electronically, was assessed. Results were summarized descriptively.

Results: Twelve out of 13 eligible hospitals participated. The overall prevalence of antimicrobial use was 30.6% (458/1499). The most common indications for antimicrobial use were respiratory tract infections (15.0%) and urinary tract infections (10.8%). Six-hundred and fifty-nine antimicrobial agents were prescribed to 458 acute care patients; a third (33.4%) of these patients received >1 antimicrobial agent. The most frequent antimicrobial agents prescribed were metronidazole (11.1%), cefazolin (10.9%), and ceftriaxone (9.0%). The majority of patients (62.1%) received antimicrobial agents by the intravenous route. Adherence to treatment guidelines was 29.9% (26/87).

Conclusions: Antimicrobial agents were prescribed to approximately 30% of acute care patients in Nova Scotia, and 62% were administered intravenously. Antimicrobial stewardship in Nova Scotia should target the potential to switch from intravenous to oral administration where appropriate, and adherence to local guidelines.

31. BACTERIAL TYROSINE PHOSPHORYLATION OF A MULTICARGO CHAPERONE REGULATES HIERARCHICAL TYPE III EFFECTOR SECRETION AND SUPPORTS ENTERIC DISEASE

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Introduction: Pathogenic *E. coli* cause serious gastrointestinal disease and inflict a significant burden on healthcare systems worldwide. The *E. coli* type III secretion system (T3SS) is a needle-like complex that mediates rapid and direct injection of multiple effector proteins into host target cells to subvert normal host signalling pathways and promote infection. Like many other pathogens, *E. coli* tightly regulate T3SS activity, which involves a variety of bacterial chaperones in the cytosol that bind to and stabilize effectors prior to their injection into a target cell. A recent phosphotyrosine proteome study of EHEC O157:H7 identified an unprecedented abundance of tyrosine-phosphorylated proteins. This reversible form of post-translational modification was previously thought to be rare among bacteria, yet was discovered to occur among proteins involved in type III secretion-mediated virulence of *E. coli*. Specifically, two consecutive tyrosine (Y) residues, Y152 and Y153, located within the unique C-terminal domain of the type III secretion chaperone (T3SC) protein known as CesT, were identified as being phosphorylated. We set out to characterize the effect of this phosphorylation on regulation of type III secretion, which critically involves CesT to promote efficient effector secretion.

Methods: *E. coli* strains deficient for CesT phosphorylation were generated with recombinant DNA mutagenesis techniques on the *cesT* allele. These CesT variants express specific Y to phenylalanine (F) substitutions, a strategy that retains protein structure but prevents phosphorylation due to absence of a critical oxygen atom on F residues. With well-established infection assays we have been able to characterize the impact of CesT phosphosite mutations on effector translocation and infection progression.

Results: CesT phosphorylation at Y152 or Y153 influences the secretion outcome for different effectors. Positional Y to F sequence changes for CesT resulted in loss of specific effector injection, and loss of phenotypes associated with disease progression *in vitro*, and *in vivo*.

Conclusions: Tyrosine phosphorylation of CesT contributes to efficient delivery of type III effectors during EPEC infection. EPEC strains deficient for CesT phosphorylation are attenuated in a variety of infection assays.

32. IL-4 ENHANCES IFN PRODUCTION BY VIRAL-INFECTED HUMAN MAST CELLS

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Introduction: Mast cells are resident in mucosal and epithelial tissues, where they serve as sentinel cells against parasitic and bacterial infections. Mast cells can also respond to multiple viruses, including respiratory viruses such as influenza A virus (IAV), reovirus, and respiratory syncytial virus through the selective production of pro-inflammatory cytokines. Allergic asthma is associated with a Th2 driven inflammation and increased susceptibility to viral infections which are the main triggers of asthma exacerbations. Interferons (IFNs) have a key role in controlling virus replication and their production has been reported to be lower in asthmatic compared to healthy subjects. Th2 cytokines may be involved in this difference in response. Mast cells have the ability to respond to Th2 cytokines and are an important source of IFNs. The objective of this work is to analyze whether mast cell IFN responses to reovirus and IAV are impaired in the presence of Th2 cytokines.

Methods: Cord blood-derived human mast cells (CBMC) were cultured in medium alone or stimulated with IL-4 (10 ng/ml), IL-5 (10 ng/ml), IL-9 (10 ng/ml), IL-13 (10 ng/ml), and IL-33 (1 ng/ml) for 48 h followed by infection with reovirus type 3 Dearing (5 MOI) or IAV (H1N1 A/CA/07/2009, 5 MOI). Supernatants were harvested 24 h p.i. for ELISA analysis. mRNA gene expression was analyzed by qPCR.

Results: IFN production by reovirus infected CBMC (Reo-CBMC) was not impaired by pretreatment with Th2 cytokines. Strikingly, IL-4 selectively enhanced the production of type I and type III IFNs. Although IL-4 and IL-13 share a common receptor, these responses were specific for IL-4. Reo-CBMC stimulated with IL-4 only concurrently with viral infection did not enhance IFN production. In addition, IL-4 pretreated CBMC showed an increased production of IL-6, CCL-3, and CXCL10 in response to reovirus. Similar to Reo-CBMC, IL-4 pretreated CBMC showed an enhanced IFN production in response to IAV.

Conclusions: Our data suggest that IL-4 modifies mast cell IFN responses when administered prior to reovirus or IAV infection. IL-4 actions on mast cells are likely to be induced through type I IL-4 receptors. We suggest that mast cells might be of importance in the control of viral infection in asthmatics by IL-4-enhanced production of IFNs, which are critical for viral clearance.

33. IMPACT OF OSELTAMIVIR IN THE PREVENTION OF SERIOUS OUTCOMES ASSOCIATED WITH INFLUENZA IN HOSPITALIZED CANADIAN ADULTS: A POOLED ANALYSIS FROM THE SERIOUS OUTCOMES SURVEILLANCE (SOS) NETWORK OF THE CANADIAN IMMUNIZATION RESEARCH NETWORK (CIRN)

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Introduction: Influenza has remained a significant cause of morbidity and mortality despite the use of effective vaccines. The objective of this study was to assess the impact of antiviral administration on the outcome of ICU admission or mechanical ventilation in hospitalized patients with laboratory-confirmed influenza.

Methods: The Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS) Network conducts active surveillance for laboratory-confirmed influenza requiring hospital admission across Canada. This study uses patients enrolled in the SOS Network during the 2011/2012-2013/14 influenza seasons who were admitted with any acute respiratory diagnosis or syndrome and tested PCR-positive for influenza. Demographic and medical information was obtained from the patient or from the medical record. The main outcome investigated was ICU admission/ mechanical ventilation. Logistic regression with backwards stepwise selection was used to estimate odds ratios (ORs) and 95% confidence limits (CIs) of ICU admission/ mechanical ventilation for the main exposure of interest (antiviral use in hospital), as well as other risk factors of interest (e.g. age, vaccination status, gender).

Results: Data were available for 4,861 patients over the three influenza seasons. The median age was 70 years (range, 16-105 years), 2535 (52%) were female, 4319 (89%) had a comorbid illness. Vaccination status was available for 4133 patients, of whom 1850 (45%) had been vaccinated for influenza in the current season. After hospital admission, 2642 (54%) of the patients were treated with antiviral therapy. 812 (17%) of patients were admitted to ICU or mechanically ventilated. Treatment with antiviral drugs was associated with a significant reduction in admission to ICU or mechanical ventilation (OR= 0.1; 95% CI: 0.1-0.1; $P = 0.000$).

Conclusions: Despite high rates of vaccination, many patients in this population are hospitalized with influenza each year. Treatment with antiviral drugs was associated with a significant reduction in ICU admission and mechanical ventilation for those admitted with influenza.

34. HIPPO PATHWAY CONTROL OF KSHV INFECTION

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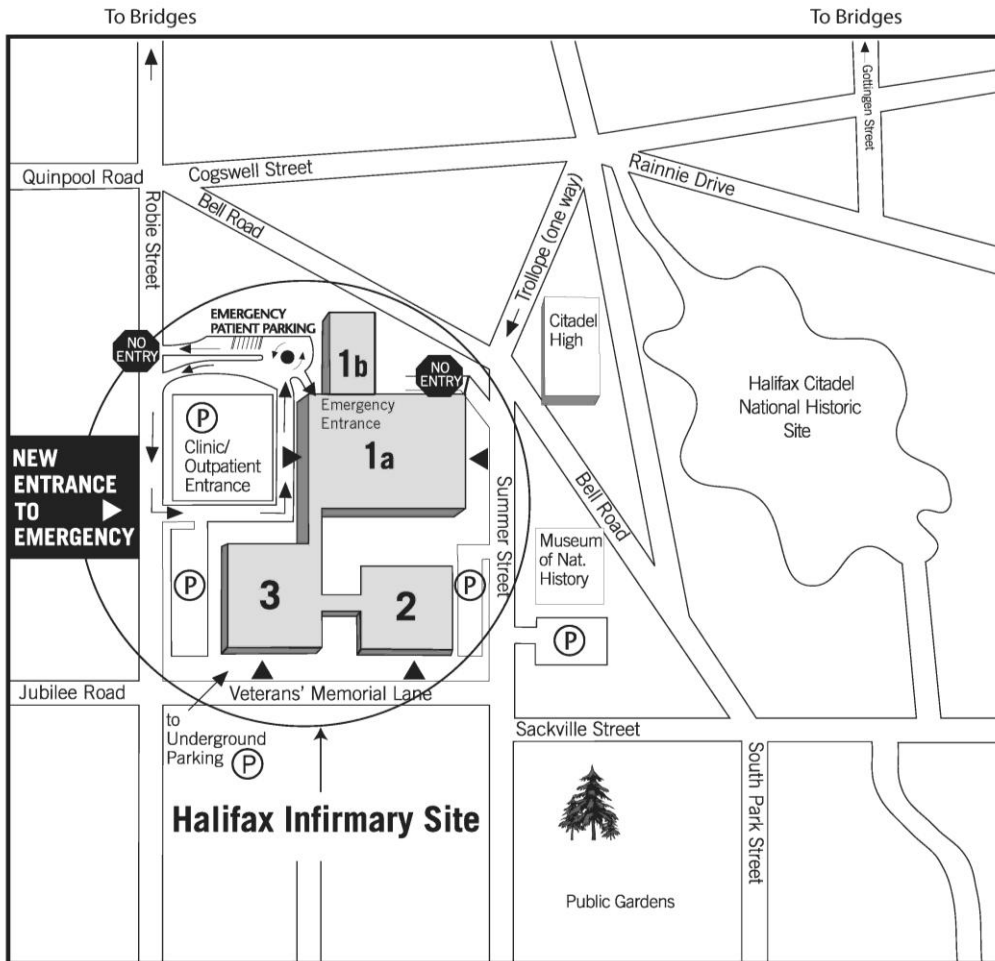
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QEII Halifax Infirmary Site (Lecture in Royal Bank Theatre)

HI Site		
1a. Halifax Infirmary	2. Abbie J. Lane Memorial Building	3. Camp Hill Veterans' Memorial Building
1b. Emergency Department		

Ⓟ Patient Parking

▶ Entrance Doors



Dalhousie University Site (Presentations held in SUB)

DALHOUSIE UNIVERSITY CAMPUS

STUDLEY CAMPUS

