24th Annual Infectious Diseases Research Day & 11th Annual Canadian Center for Vaccinology Symposium

DALHOUSIE UNIVERSITY
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Canadian Center for Vaccinology
Dalhousie University
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April 30, 2019
Halifax, Nova Scotia

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Dalhousie Divisions of Infectious Diseases
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In keeping with CMA Guidelines, program content and selection of speakers are the responsibility of the planning committee. Support is directed toward the costs of the course and not to individual speakers through an unrestricted educational grant.

Thank you!

This program is supported in part by contributions-provided by:

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The Infectious Diseases Research Day and CCfV Symposium is a unique learning opportunity featuring experienced presenters and research trainees. Our program this year is filled with a variety of presentations and posters, from basic science to policy and programs.

After the positive response from last year's program, we are excited to again offer a networking wine and cheese event following the award presentations. I hope you will take this opportunity to unwind, talk with colleagues, ask questions, and learn as much as you can about the process and results of research.

Feedback and evaluation is extremely important, and you are the key to that process! 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 this learning event.

Scott Halperin MD, FRCPC
Director
Canadian Center for Vaccinology

The Infectious Diseases Research Day and CCfV Symposium is an event I look forward to each year, where trainees and established researchers are able to present their results and learn from their colleagues.

Providing continuing education credits via the Dalhousie University Continuing Professional Development has been an important feature of attending this event for years. But, for this first time we are proud to offer 7 Continuing Education Units from the Dalhousie Continuing Pharmacy Education office to the pharmacists in attendance. Pharmacist continue to play a vital role in immunization research, and we are excited to offer this continuing education opportunity for them.

I offer my sincere thanks to our planning committee and the financial support from our corporate sponsors. Without their continued support and hard work, this event would not be possible.

Program

24th Annual Infectious Diseases Research Day &
11th Annual Canadian Center for Vaccinology Symposium

Tuesday April 30, 2019

8:00-9:00am	TJ Marrie Lecture- Jennifer Gardy,*Ten Years and Two Thousand Genomes Later: Lessons Learned from Tuberculosis Genomics in BC*	Halifax Infirmary RB Theatre
9:30–12:30pm	Oral Presentations (10)	Dalhousie University McInnes Room
12:30–1:15pm	Lunch	
1:00–2:00pm	Poster judging (posters on display 1:00 – 5:30)	Dalhousie University McInnes Room
2:00–3:00pm	Presentation – Julie Bettinger, *Implementation Vaccinology: vaccine effectiveness, safety and hesitancy research*	Dalhousie University McInnes Room
3:00-3:15	Nutrition Break	
3:15–3:45pm	Presentation – Alyson Kelvin, *"Influenza Vaccination and Immune History -- I was sick last year, should I be vaccinated this year"*	Dalhousie University McInnes Room
3:45-4:15pm	Presentation – Matthew Herder, *"The Merck [sic] Ebola Vaccine & Precarious Public Sector Science"*	Dalhousie University McInnes Room
4:15-4:30pm	Awards Presentations	Dalhousie University McInnes Room
4:30-5:30pm	Networking/Mentoring Wine and Cheese	Dalhousie University McInnes Room

Educationally co-sponsored by Dalhousie University Continuing Professional Development

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

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Speakers

Dr. Jennifer Gardy

Dr. Jennifer Gardy joined the Bill & Melinda Gates Foundation's malaria team as Deputy Director, Surveillance, Data, and Epidemiology in February 2019. Before that, she spent ten years at the BC Centre for Disease Control and the University of British Columbia's School of Population and Public Health, where she held the Canada Research Chair in Public Health Genomics.

Her research focused on the use of genomics as a tool to understand pathogen transmission, and incorporated techniques drawn from genomics, bioinformatics, modelling, information visualization, and the social sciences. In 2018, Jennifer was named one of BC's Most Influential Women in STEM by BC Business Magazine, and was named of the Government of Canada's 20 Women of Impact in STEM.

Dr. Julie Bettinger

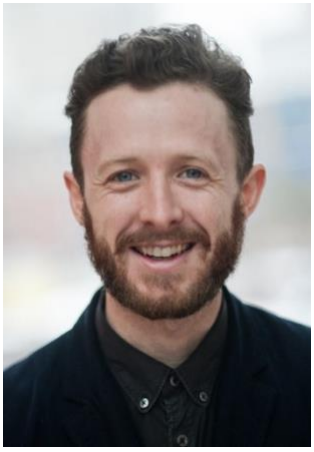
Dr. Julie Bettinger is a vaccine safety scientist at the Vaccine Evaluation Center, a leading center for applied vaccine research in Canada. Her research interests include vaccine safety, vaccine hesitancy and vaccine preventable diseases, as well as attitudes and beliefs around immunization uptake and use.

Dr. Bettinger is also the epidemiologist for the Immunization Monitoring Program, Active, a national surveillance system for vaccine preventable diseases and vaccine adverse events in 12 pediatric tertiary care centers across Canada and the lead investigator for the Canadian National Vaccine Safety (CANVAS) network, an active surveillance network that monitors the safety of vaccines.

Dr. Alyson Kelvin

Dr. Alyson Kelvin is a virologist at the IWK Health Centre, Canadian Centre for Vaccinology, and Dalhousie University. Her research aims to identify the mechanisms that regulate *viral imprinting* for use in informed vaccine design. Much of her work focuses on influenza viruses. These viruses are a recurrent and as yet unsolved public health problem. The main problem is that vaccines to prevent infection are not 100% effective. To address this problem, Dr. Kelvin's current NIH and NSHRF projects investigate how previous exposure to influenza viruses influence subsequent vaccination responses.

Using the enemy's strength to our advantage –Dr. Kelvin contends that understanding the mechanisms of viral imprinting and immune recall during recurrent host-virus interactions will be key to effectively designing the universal influenza vaccine.



Matthew Herder

Matthew Herder is the Director of the Health Law Institute at Dalhousie University, and an Associate Professor in the Department of Pharmacology in the Faculty of Medicine. Prof. Herder's research focuses on biomedical innovation policy and is supported by grants from the Canadian Institutes of Health Research, the Royal Society of Canada, and the Commonwealth Fund. His scholarship and advocacy has significantly helped to improve the transparency of pharmaceutical regulation in Canada. In 2018 he was appointed by the federal cabinet to serve a five-year term as a member of the Patented Medicine Prices Review Board, Canada's national drug price regulator.

Poster Presentations

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

22	**M Surette,** A Mayavannan, J Wang. THE EFFECTS OF AID GENE KNOCKOUT ON *CHLAMYDIA MURIDARIUM* IMMUNOPATHOLOGY	35
23	**C Taylor,** N MacDonald, L Menning, C M McMurtry, O Benes, M Balakrishnan, M Gold. IMMUNIZATION STRESS RELATED RESPONSES (ISRRs)	36
24	**T Canning,** V Murphy, R Davidson, P Bonnar. OPTIMIZNG TREATMENT OF BLOODSTREAM INFECTIONS: IMPACT OF ANTIMICROBIAL STEWARDSHIP INTERVENTION FOLLOWING FINAL SUSCEPTIBILITY REPORT	37

Oral Presentations

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

		Oral Abstract	Page
9:30-9:45	**J J LeBlanc,** M ElSherif, L Ye, D MacKinnon-Cameron, A Ambrose, T F Hatchett, I Martin, M K Andrew, G Boivin, W Bowie, K Green, J Johnstone, M Loeb, A McCarthy, A McGeer, M Semret, S Trottier, L Valiquette, D Webster, S A McNeil, on behalf of the Serious Outcomes Surveillance (SOS) Network of the Canadian Immunization Research Network (CIRN). IS STREPTOCOCCUS PNEUMONIAE SEROTYPE 3 MASKING PCV13-MEDIATED HERD IMMUNITY IN ADULTS HOSPTALIZED WITH COMMUNITY ACQUIRED PNEUMONIA?	1	38
9:45-10:00	**E S Pringle,** C McCormick. COMPOSITION OF KSHV RIBONUCLEOPROTEIN COMPLEXES	2	39
10:00-10:15	**H MacKinnon,** K Slayter, J Comeau, M Science, K Timberlake, E Black. DEVOLOPMENT OF QUALITY INDICATORS TO EVALUATE APPROPRAITE EMPIRIC ANTIMICROBIAL USE IN PEDIATRIC PATIENTS	3	40
10:15-10:30	**N Ozog,** A Steenbeek, J Curran, N Kelly. ATTITUDES TOWARD INFLUENZA VACCINATION DURING 'WAIT TIMES' IN THE EMERGENCY DEPARTEMENT	4	41
10:30-10:45	**A Mayavannan,** E Shantz, A Edgar, R Clarke, G Rooke, I Haidl, J Marshall, J Wang. TLR2 EXPRESSING BONE MARROW DERIVED LEUKOCYTES INDUCE T_H17 RESPONSE IN *CHLAMYDIA* GENITAL INFECTION	5	42
10:45-11:00	**BREAK**		

11:00-11:15	**P Slaine,** M Kleer, M Roberge, A Balgi, I Haidl, N Smith, D Khaperskyy, C McCormick. HOST-TARGETED ANTIVIRALS BLOCK INFLUENZA VIRUS REPLICATION	6	44
11:15-11:30	**K Weagle,** T Manca, M Kervin, N MacDonald, K Top, J Graham. HEALTHCARE PROVIDER UNDERSTANDING OF VACCINE PRODUCT MONOGRAPHS	7	45
11:30-11:45	**D Medina-Luna,** G Gamage, M Scur, H Zein, B D Parsons, A P Makrigiannis. NK CELL MEMORY RESPONSE IN CANCER IMMUNOTHERAPY	8	46
11:45-12:00	M M A Rahim, E Price, B Chilvers, H Ajami, H Zein, P Slaine, D Medina-Luna, G Seaton, **B D Parsons**, D Khaperskyy, C McCormick, A P Makrigiannis. DEFINING MECHANISMS BY WHICH INFLUENZA ALTERS SURFACE EXPRESSION OF MHC-I	9	47
12:00-12:15	**M Francis,** M King, J Marshall, C McCormick, A Kelvin. INVESTIGATION OF THE INFLUENCE OF HOST IMMUNE HOSTORY ON THE OUTCOME OF INFLUENZA VIRUS VACCINATION IN A PREIMMUNE MOUSE MODEL	10	48
12:15	**LUNCH**		

Poster Abstracts

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

Poster 1. INFLUENZA BURDEN OF DISEASE AND PRELIMINARY 2017/18 END-OF-SEASON INFLUENZA VACCINE EFFECTIVENESS ESTIMATES FOR PREVENTING INFLUENZA-ASSOCIATED HOSPITALIZATION AMONG CANADIAN ADULTS: AN UPDATE FROM THE CIRN SERIOUS OUTCOMES SURVEILLANCE (SOS) NETWORK

Authors: SA McNeil, **MK Andrew,** T Hatchette, A Ambrose, G Boivin, M ElSherif, J Johnstone, K Katz, J Leblanc, M Loeb, D MacKinnon-Cameron, AE McCarthy, JE McElhaney, A McGeer, M Nichols, A Poirier, J Powis, D Richardson, M Semret, D Smyth, S Trottier, L Valiquette, D Webster, L Ye on behalf of the CIRN SOS Network investigators and the Toronto Invasive Bacterial Diseases Network (TIBDN) investigators

Affiliation: CCfV

Introduction: Influenza surveillance is important in order to understand patterns of disease burden and vaccine effectiveness (VE). In Canada, the Serious Outcomes Surveillance (SOS) Network conducts active surveillance for influenza hospitalizations at 13 adult and community hospitals in four provinces (Ontario, Quebec, New Brunswick and Nova Scotia). We contribute these Canadian data to the Global Influenza Hospital Surveillance Network (GIHSN).

Methods Active surveillance for influenza infection in adults (≥16 years of age) was conducted January 1st to April 30th, 2018. For laboratory confirmation, all patients with acute respiratory illness or unexplained sepsis had nasopharyngeal swab PCR testing for influenza A & B. Clinical and demographic data included age, vaccination status and frailty. Comparing influenza cases with test-negative controls, VE was calculated as VE = 1-OR x 100%. This preliminary unmatched VE analysis was presented at the annual GIHSN meeting in October, 2018.

Results: 2063 lab-confirmed influenza cases were enrolled in the SOS Network during the 2017-2018 influenza season. Influenza A was the predominant strain (55.2%), though there was substantial circulation of influenza B throughout the season. Most patients were older adults, with 55.6% being aged 75+. Half of the patients were at least mildly frail. Overall, 11.3% of patients with laboratory-confirmed influenza were admitted to ICU and 6.4% died. ICU admission generally decreased with increasing frailty, while mortality increased. The overall preliminary VE estimate was 42.1%. Notably, VE was higher in older adults (65+) at 47.1% vs. 24.0% for adults under age 65.

Conclusions: The SOS Network contributes to influenza surveillance (informing understanding of burden of disease and vaccine effectiveness) in Canada, and also contributes importantly to global surveillance efforts through the GIHSN. The SOS Network's continued focus on outcomes and health measures relevant to older adults (particularly frailty and function) continues to contribute to our understanding of influenza in this important and vulnerable population.

Poster 2. PERFORMANCE OF TWO EIA ALGORITHM FOR LYME DISEASE (LD) IN NOVA SCOTIA

Authors: **Davis I[1,2]**, McNeil SA[1,2,4], Allen W[4], MacKinnon-Cameron D[4], Wilson, K[2], Lindsay R[3], Dibernardo A[3], Hatchette TF[1,2,4]

Affiliation: 1Nova Scotia Health Authority (NSHA), and 2Dalhousie University, Halifax, NS; 3National microbiology Laboratory, Public Health Agency of Canada; 4Canadian Center for Vaccinology

Introduction: US data suggests that a two EIA algorithm (2EIA) (whole cell (WC) EIA followed by C6 EIA) has improved sensitivity but equivalent specificity to the recommended two tier algorithm (TTA) (EIA followed by Western blot (WB)) for the serologic diagnosis of LD. From 2010 to 2014, the QEII laboratory used a WC EIA for LD serology. Positive or indeterminate results were then tested with the C6 EIA by the National Microbiology Laboratory. Only the sera with positive or equivocal C6 results were tested with IgG and IgM WB, providing the opportunity to evaluate the real world performance of the 2EIA compared to TTA in a Nova Scotian population.

Methods: A retrospective chart review was performed on patients testing positive with both WC and C6 (2EIA approach). Patients were classified as having LD if they had 1. a positive TTA result; 2. A negative TTA result but had symptoms consistent with LD; or 3. Evidence of seroconversion between consecutive specimens. Specificity was calculated based on standard 4x4 table.

Results: From 2010-2014, 10253 specimens were tested for LD, 9806 were negative. Of the 271/447 positive charts reviewed to date, 226 and 45 specimens were classified as coming from patients with and without LD respectively. The number of 2EIA positive patients without LD (false positive results) was 45. Of the 226 with LD 158 had current infection. Of these 88 had positive IgG WB; 49 positive IgM WB with negative IgG WB; 21 negative specimens with IgG/IgM WBs. Calculated specificity is 99.53% (99.38-99.66%).

Conclusions: Preliminary analysis suggests the 2EIA has excellent specificity and is more sensitive than the TTA. A further chart review is required to accurately define the sensitivity of 2EIA in our population.

Poster 3. LONG-TERM CARE ADMISSIONS FOLLOWING HOSPITALIZATION: THE ROLE OF SOCIAL VULNERABILITY

Authors: **J Godin**, K Black, O Theou, McNeil SA, Andrew MK on behalf of the CIRN SOS Network Investigators

Affiliation: Medicine (Geriatrics and ID)

Introduction: Social vulnerability is the extent overall social circumstances leave individuals susceptible to negative health outcomes. We sought to understand the association between social vulnerability and the odds of long-term care (LTC) placement within 30 days of discharge following admission to an acute care facility and whether this association varied based on age, sex, or baseline frailty.

Methods: Patients admitted to hospital with acute respiratory illness were enrolled in the Canadian Immunization Research Network's Serious Outcomes Surveillance Network during the 2011/2012 influenza season. Participants (N=475) were 65 years or older (Mean=78.6) and over half were women (58.9%). Social vulnerability was measured using a Social Vulnerability Index (SVI) and frailty was measured with a Frailty Index (FI). Due to the rarity of incident LTC placement (N=15), we used penalized likelihood logistic regression.

Results: At age 65, social vulnerability was associated with lower odds of LTC placement at high levels of frailty (FI = 0.4; OR=0.15, 95%CI=0.03-0.61), but not at lower levels of frailty. At age 85 social vulnerability was associated with greater odds of LTC placement in the fittest patients (FI =0.0; OR=13.54, 95%CI=1.42, 131.76 and FI =0.1; OR=6.71, 95%CI=1.01, 40.43), but not at higher levels of frailty. Various sensitivity analyses yielded similar results.

Conclusions: Social vulnerability interacted with frailty and age. Perhaps the reason that social vulnerability was associated with lower odds of LTC placement in younger, frail patients is that, although these frailer participants might be in need of LTC, they do not have anyone advocating for them. In contrast, social vulnerability was associated with greater odds of LTC placement in older patients who were fitter but there was no difference among those who were frailer, suggesting that at a certain age and frailty level, LTC placement is difficult to avoid even with a supportive social situation.

Poster 4. VALIDATION OF THE SEEGENE RV15 MULTIPLEX PCR FOR THE DETECTION OF INFLUENZA A SUBTYPES AND INFLUENZA B LINEAGES DURING NATIONAL INFLUENZA SURVEILLANCE IN HOSPITALIZED ADULTS

Authors: **J. J. LeBlanc[1],** M. ElSherif[1], S. Mulpuru[2], M. Warhuus[1], A. Ambrose[1], M. Andrew[1], G. Boivin[3], W. Bowie[4], A. Chit[5,6], G. Dos Santos[7], K. Green[8], S. A. Halperin[1], T.F. Hatchette[1], B. Ibarguchi[9], J. Johnstone[10], K. Katz[11], J. M. Langley[1], P. Lagacé-Wiens[12], M. Loeb[10], A. Lund[1], D. MacKinnon-Cameron[1], A. McCarthy[22], J. E. McElhaney[13], A. McGeer[8], A. Poirier[14], J. Powis[15], D. Richardson[16], M. Semret[17], V. Shinde[18], D. Smyth[19], S. Trottier[3], L. Valiquette[20], D. Webster[21], L. Ye[1], S. A. McNeil[2], on behalf of the Serious Outcomes Surveillance (SOS) Network of the Canadian Immunization Research Network (CIRN)

Affiliation: [1]Canadian Center for Vaccinology, Dalhousie University, IWK Health Centre, and Nova Scotia Health Authority, Halifax, NS; [2]Ottawa Hospital Research Institute, University of Ottawa, ON; [3]Centre Hospitalier Universitaire de Québec, QC; [4]University of British Columbia, Vancouver, BC; [5]Sanofi Pasteur, Swiftwater, Pennsylvania, USA; [6]Leslie Dan Faculty of Pharmacy, University of Toronto, ON; [7]Business & Decision Life Sciences [on behalf of GSK], Bruxelles, Belgium (Current affiliation: GSK, Wavre, Belgium); [8]Mount Sinai Hospital, Toronto, ON; [9]GSK, Mississauga, ON (Current affiliation: Bayer Inc. Mississauga, Ontario, CA); [10]Public Health Ontario and University of Toronto, ON; [11]North York General Hospital, Toronto, ON; [12]St. Boniface Hospital, Winnipeg, MB; [13]Health Sciences North Research Institute, Sudbury, ON; [14]Centre Intégré Universitaire de Santé et Services Sociaux, Quebec, QC; [15]Toronto East General Hospital, Toronto, ON; [16]William Osler Health System, Brampton, ON; [17]McGill University, Montreal, QC; [18]GSK, King of Prussia, Pennsylvania, USA (Current affiliation: Novavax Vaccines, Washington, DC, USA); [19]The Moncton Hospital; Moncton, NB; [20]Université de Sherbrooke, Sherbrooke, QC; [21]Horizon Health, Saint John, NB; [22]Ottawa Hospital General, Ottawa, Ontario, Canada.

Introduction: The Serious Outcomes Surveillance Network of the Canadian Immunization Research Network (CIRN SOS) has been performing active influenza surveillance since 2009. Influenza A and B viruses are identified and characterized using real-time RT-PCR, and on a subset of patients, multiplex testing was performed to identify other respiratory virus etiologies. Since both methods could identify influenza A and B, a direct comparison was performed.

Methods: Validated real-time RT-PCRs from the World Health Organization (WHO) to identify influenza A and B viruses, characterize influenza A viruses into the H1N1 or H3N2 subtypes, and to describe influenza B viruses belonging to the Yamagata or Victoria lineages. In a subset of patients, the Seeplex RV15 One-Step ACE Detection assay (RV15) kit was also used for detection of other respiratory viruses.

Results: In total, 1111 nasopharyngeal swabs were tested by RV15 and real-time RT-PCRs for influenza A and B identification and characterization. For influenza A, RV15 showed 98.0% sensitivity, 100% specificity, and 99.7% accuracy. Performance characteristics of RV15 were

similar for Influenza A subtypes H1N1 and H3N2. For influenza B, RV15 had a 99.2% sensitivity, 100% specificity and 99.8% accuracy, with similar assay performance for both the Yamagata and Victoria lineages.

Conclusions: Overall, detection of circulating subtypes of influenza A and lineages of influenza B by RV15 was similar to real-time RT-PCR. Multiplex testing with RV15 allows for a more comprehensive assessment of respiratory virus surveillance in hospitalized adults, without significantly compromising the reliability of influenza A or B virus detection.

Poster 5. DEFINING MINIMALLY IMPORTANT DIFFERENCES FOR THE FRAILTY INDEX IN A LONGITUDINAL CLINICAL COHORT OF HOSPITALIZED OLDER PATIENTS

Authors: A van der Valk, O Theou, J Godin, MK Andrew, JE McElhaney, **SA McNeil**, K Rockwood

Affiliation: Medicine (Geriatrics and ID)

Introduction: The minimally important difference (MID) of the frailty index (FI) can be useful for guiding patient treatment but has yet to be explored. This study aims to establish MIDs for the FI by associating changes in FI scores to changes in the Clinical Frailty Scale (CFS).

Methods: Since 2009, the CIRN Serious Outcomes Surveillance (SOS) Network has collected longitudinal health data from patients admitted with acute respiratory illness to 10-45 hospitals across Canada during influenza season. Here, we analyzed frailty data (CFS, FI) from 6,063 patients (M_{age}=79.6 ± 8.4 years; 52.8% female) at pre-admission, admission, and 30 days post-discharge. We constructed a 39-item deficit accumulation FI. We identified the mean change in FI associated with a one-level increase in CFS scores from baseline to admission and one-level decrease in CFS scores from admission to post-discharge. We also examined the value of FI change with the highest sensitivity and specificity (Youden Index (*J*)) in predicting one-level CFS change.

Results: Overall, 96.7% of participants had a higher CFS score at admission compared to pre-admission; 70% improved their CFS level from admission to discharge. The average FI change among patients who changed their CFS score by one level was 0.06 ± 0.06. An FI change of 0.03 best predicted both one-level CFS increases (*J*=0.27; sensitivity=67%; specificity=61%) and decreases (*J*=0.40; sensitivity=71%, specificity=69%). For those whose CFS scores increased from preadmission to admission, 70.4% increased their FI by ≥0.03. For those whose CFS scores improved from admission to post-discharge, 72% decreased their FI by ≤-0.03.

Conclusions: In a 39-item FI, an MID of 0.03 (a ~1 deficit change) is a promising benchmark for improving clinical assessment of the efficacy of frailty interventions.

Poster 6. A DISK-DIFFUSION METHOD FOR THE DETECTION OF CEFAZOLIN INOCULUM EFFECT IN METHICILLIN-SUSCEPTIBLE *STAPHYLOCOCCUS AUREUS*

Authors: Glenn Patriquin[1, 2], Hilal Al Sidairi[1,2], Joline Head[2], Jason LeBlanc[1,2], Ian Davis[1,2], Ross Davidson[1,2], Zafar Hussain[2,3]

Affiliation: [1]Dalhousie University, [2]Nova Scotia Health Authority, [3] University of Western Ontario

Introduction: Cefazolin has excellent activity against methicillin-susceptible *Staphylococcus aureus* (MSSA), but some strains show cefazolin inoculum effect (CzIE) which may reduce the clinical effectiveness of this drug. Currently, MSSA strains with CzIE are identified by the micro broth dilution method (MBDM) using a high inoculum, but this method is cumbersome and cannot be used routinely. This study sought to evaluate a more simple method to identify MSSA with CzIE using standard disk diffusion method (DDM).

Methods: 203 non-duplicated MSSA isolated from blood cultures were evaluated. The cefazolin MIC was determined by the MBDM using the standard inoculum (10^5 colony forming units (CFU)/mL) and high inoculum (10^7 CFU/mL). MBDM testing was performed according to CLSI guidelines. A *S. aureus* reference strain exhibiting CzIE was provided as a kind gift from Dr. Barbara Murray (Houston, Texas) and was used as a control. CzIE was defined as an increase in MIC to cefazolin >16 mg/L when tested with the high inoculum. Zones of inhibition for cefazolin were determined by DDM using a 30mg cefazolin disk as per CLSI guidelines.

Results: Of 203 MSSA isolates, 64 had a cefazolin MIC of ≥16 mg/L using high inoculum, thus were positive for CzIE. One hundred thirty-nine strains did not show CzIE using MBDM. Using a zone of ≤30 mm as a cut-off, the sensitivity of cefazolin DDM was 92.2% (59/64), but the specificity was low at 66.9% (93/139).

Conclusions: This study shows that the DDM of cefazolin is reasonably sensitive for identifying MSSA with CzIE. The method is easy to perform and may identify patients for whom cefazolin may not be an optimal drug. Further analyses are underway to validate the robustness of these conclusions.

Poster 7. APPLYING SYNTHETIC BIOLOGY TECHNIQUES TO THE STUDY OF KAPOSI'S SARCOMA-ASSOCIATED HERPESVIRUS

Authors: B. A. Duguay[1,2], D. Knight[1] , M. Thornbury[1] , J. R. Rohde[1,3], C. McCormick[1,2,3]

Affiliation: [1]Dalhousie University, [2]Beatrice Hunter Cancer Research Institute, [3]Canadian Centre for Vaccinology

Not published by request.

Poster 8. HOST SCAFFOLD PROTEIN, RACK1, IS REQUIRED FOR *SHIGELLA FLEXNERI* INVASION AND CELL-TO-CELL SPREADING

Authors: **K Valenzuela,** J Rhode, J Enninga, Z Cheng

Affiliation: [1]Dalhousie University, microbiology and immunology. [2]Pasteur Institute, Dynamics of Host-Pathogen Interactions, Paris, France.

Introduction: *Shigella flexneri* is a Gram-negative intracellular bacterium that infects human colonic epithelial cells, causing inflammatory colitis. *S. flexneri* induces host actin polymerization at the entry site to promote bacterial uptake. Once within the cell, this pathogen induces polymerization of an actin tail that propels the bacterium, allowing cell-to-cell spreading. The receptor for activated C kinase 1 (RACK1) is a scaffolding protein that provides a platform for protein-protein interactions, playing pivotal roles in cell homeostasis maintenance. For example, RACK1 binds to components of the actin cytoskeleton, allowing focal adhesion assembly and cell migration. Considering that *S. flexneri* usurps host cell actin cytoskeleton and that RACK1 interacts with the cytoskeleton machinery, we hypothesize that *S. flexneri* requires RACK1 to invade and spread in host cells.

Methods: To evaluate the role of RACK1 during *S. flexneri* infection. RACK1 expression was silenced in HeLa cells using lentiviral shRNA. *S. flexneri* intracellular growth in control (shNS) and RACK1 silenced (shRACK1) HeLa cells was assessed by quantification of bacterial colony forming units. Number of infected cells, number of bacterial entry sites, actin tail formation and cell-to-cell spreading were evaluated by immunofluorescence (IF) and live microscopy (LM).

Results: Significantly less *S. flexneri* were recovered from shRACK1 cells compared to control cells. The number of infected cells and number of bacterial entry sites per cell significantly decreased in shRACK1 cells. IF experiments showed 50% less intracellular bacteria associated with actin tails in shRACK1 cells compared to control. LM measurements of *S. flexneri* intracellular motility showed significantly reduced bacterial speed and cell-to-cell spreading in shRACK1 cells compared to control cells.

Conclusions: RACK1 silencing is detrimental to *S. flexneri* growth in HeLa cells, suggesting that this pathogen requires RACK1 to infect the host. RACK1 is required for efficient *S. flexneri* invasion, actin tail formation and cell-to-cell spreading in HeLa cells. These data contribute to the understanding of the mechanisms by which *S. flexneri* exploits the host cellular machinery to sustain its intracellular life style.

Poster 9. MECHANISTIC INSIGHT INTO BACTERIAL HTPG-HOST INTERACTIONS IN CROHN'S DISEASE

Authors: **E. Finlayson-Trick,**[1] J. Connors,[2] K. Dunn,[3] A. Stadnyk,[1,4] J. Van Limbergen[1,4]

Affiliation: [1]Department of Microbiology and Immunology, Dalhousie University, Halifax, NS, [2]Canadian Center for Vaccinology, IWK Health Centre, Halifax, NS

Introduction: Increased expression of specific heat shock proteins (HSPs) in patients with Crohn's disease (CD) protects intestinal epithelial cells from stress. Previously, we observed increased levels of the bacterial HSP, high temperature protein G (HtpG), in pediatric CD patients able to sustain remission following treatment with exclusive enteral nutrition (EEN). HtpG is the bacterial homolog to eukaryotic HSP90. Only two out of the three HtpG lineages (Groups A and B) are observed clinically. Recently, we observed that application of *Bacteroides fragilis* (*B. fragilis*) HtpG to TNF-inflamed colonic epithelial cells reduced expression of CXCL8. The mechanism by which HtpG modulates intestinal epithelial cell responses remains unclear. We hypothesize that as HSP90 is known to interact with the CD-associated protein NOD2 and as HSP90 and HtpG are homologous, HtpG may also interact with NOD2.

Methods: HtpG relative abundance and sequences were pulled for each patient from our published metagenomic dataset. Sequences were run through the BLAST database and aligned using Clustal Omega. Trees showing HtpG Group distribution were generated from amino acid sequences using RAxML. HEK293T cells were transfected with Group B *B. fragilis* 6x-His-HtpG and/or wild-type Flag-NOD2. Lysates were collected and cobalt bead affinity purified. The purification was analyzed via SDS-PAGE probed with α-His and α-NOD2 antibodies.

Results: Preliminary data suggests that the relative abundance of HtpG increased during and post-EEN but that the diversity of bacterial genera contributing the signal decreased. The distribution of HtpG amongst Groups A and B did not change significantly. A 70kDa species corresponding to 6xHis-HtpG bound efficiently to the column and was recovered by competitive elution. Precipitation of 6xHis-HtpG aided in the recovery of Flag-NOD2 as determined by the appearance of a 100kDa species via NOD2 immunoblot.

Conclusions: We observed that bacterial diversity may not necessarily correspond to HtpG abundance or distribution, suggesting that EEN may place metabolic pressures on certain bacterial genera to produce more/less HtpG. We also observed a potential interaction between the bacterial chaperone HtpG and human NOD2. Further downstream analysis is required to confirm the interaction.

Poster 10. ALTERNATIVE TRANSLATION INITIATION DURING KSHV INFECTION

Authors: C Munoz, K Top for the Special Immunization Clinic Network Investigators

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Introduction: Adverse events following immunization (AEFI) are any untoward medical occurrence following vaccination which do not necessarily have a causal relationship with a vaccine. Many patients who experience an AEFI still require further vaccinations. The aim of this thesis proposal is to identify predictors of revaccination and AEFI recurrence in patients with AEFI history. Our objectives are to identify predictors of: (1) physician recommendations for revaccination, (2) patient acceptance of revaccination and (3) AEFI recurrence in this population.

Methods: This is a retrospective analysis of data collected on Special Immunization Clinic (SIC) network patients with history of AEFI from 2013-2018. We will measure frequency of clinician recommendation for revaccination, patient acceptance of revaccination and frequency AEFI recurrence following revaccination with the vaccine associated with the initial AEFI. We will use descriptive statistics and multivariable regression analysis to identify and measure predictors of revaccination acceptance and AEFI recurrence outcomes (e.g., age, sex, AEFI type, severity, vaccine, allergy test and causality). Data will be extracted from DACIMA electronic database and uploaded to STATA (V.15.1) for analysis.

Results: From 2013-2018, the SIC enrolled 671 patients of whom 535 have a history of AEFI. Of SIC patients, 90% are children, 50% are male, and 72% have been revaccinated. Currently, I am writing my thesis proposal, reviewing literature and cleaning the SIC research database.

Conclusions: Our goal is to improve patient care through maintaining safety during revaccination in patients with previous AEFI history and ensure that patients are receiving all the vaccines they need to be protected against infectious diseases.

Poster 11. CORRELATION BETWEEN THE MIC OF VANCOMYCIN AND THOSE OF OTHER AGENTS AGAINST METHICILLIN-SUSCEPTIBLE STAPHYLOCOCCUS AUREUS RECOVERED FROM BLOODSTREAM INFECTIONS

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Introduction: The minimum inhibitory concentration (MIC) of vancomycin has been used as a marker for the response to anti-staphylococcal penicillins in methicillin-susceptible Staphylococcus aureus (MSSA) bacteremia. This study evaluated whether an increase in vancomycin MIC in MSSA isolates would be associated with a concurrent rise in the MIC of the other antibiotics used to treat MSSA bacteremia, including telavancin, daptomycin, oxacillin and cefazolin.

Methods: 305 MSSA strains recovered from hospitalized patients with bacteremia were tested for their susceptibility to vancomycin, telavancin, daptomycin, oxacillin and cefazolin by the Etest according to the manufacturer's instructions. MIC range, MIC mean, MIC50, MIC 90 and MIC 100 for all antibiotics tested were recorded, and data was categorized according to vancomycin MIC (0; 0.75; 1.0; 1.5; and 2.0) or oxacillin MICs (0.038, 0.094, 0.125, 0.19, 0.25, 0.38, 0.5, 0.75, 1.0, and 1.5) to evaluate the effect on MICs to other antibiotics tested

Results: When the MICs of the comparator antibiotic stratified by vancomycin MIC, a positive association in both means and ranges of telavancin and daptomycin were noted, but no associated was seen between vancomycin and oxacillin or cefazolin. However, when MSSA isolates were stratified by oxacillin MICs, the MICs for cefazolin followed the same trend, but not telavancin or daptomycin.

Conclusions: This experiment proved a rise in vancomycin MIC of MSSA is associated with a parallel rise in the MIC of telavancin and daptomycin, and that an increase in MIC to oxacillin in associated with a parallel rise in MIC to cefazolin. Physicians should be aware of these associations when treating MSSA with increasing MICs to vancomycin or oxacillin. Clinical outcomes analyses are underway in cases fitting MSSA bacteremia with elevated MICs to vancomycin or oxacillin.

Poster 12. PRACTICE VARIABILITY IN MANAGEMENT OF GRAM *B* NEGATIVE BACTEREMIAS

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Affiliation: **Division of Infectious Disease, Dalhousie University**

Introduction: There has been evolving literature on the appropriate duration and step down to oral therapy for the treatment of Gram-negative bacteremias. The primary objective of this study was to describe the practice variability in management of Gram-negative bacteremias in patients who did and did not have an infectious diseases (ID) consult.

Methods: This was a retrospective cohort study of adult patients admitted to hospital between December 2014–2017, who had a bacteremia with a non-multiple drug resistant Gram-negative bacteria. Exclusion criteria included death, discharge, or change to palliative status within 48 hours of positive culture. Febrile neutropenia, endocarditis, and graft infection patients were also excluded. In addition to descriptive statistics, chi-square test and Student t test were performed as appropriate.

Results: One hundred and sixty patients were enrolled, with 21.9% (n=35) having an ID consult. The average age was 68.6±15.7 years, with 54.4% (n=87) being male. Community-acquired bacteremia was most common (71.3%, n=114), followed by hospital (18.8%, n=30) and long term care (10.0%, n=16) associated infections. The most common microorganism was *Escherichia coli* (n=83) followed by *Klebsiella species* (n=27), with genitourinary source the most frequent etiology (n=85). Piperacillin/tazobactam was the initial antibiotic in 41.9% (n=67) of patients. Total days of therapy averaged 16.5±5.7 versus 13.9±5.1 in patients with and without an ID consult, respectively (p=0.024). Intravenous therapy was provided for a longer duration in the ID consult group (9.7±7.4 versus 5.8±4.0 days, p=0.004). Both in-hospital mortality and length of stay were similar in both groups. Readmissions to hospital at 30 days were not statistically significant between the two groups.

Conclusions: Practice patterns in regards to total duration of therapy and proportion of therapy provided intravenously were similar in patients with uncomplicated Gram-negative bacteremias with and without an ID consult. As well, patient outcomes were not statistically different. The majority of patients were treated initially with broad spectrum agents with total durations longer than 7 days.

Poster 13. LXRα ACTIVATION INHIBITS HERPESVIRUS NUCLEAR EGRESS

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Not published by request.

Poster 14. HOST INFLUENZA HISTORY DICTATES VACCINE RESPONSES THROUGH A MEMORY B CELL MECHANISM

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Introduction: The influenza virus re-emerges every year as a different virus to infect naïve human populations and cause disease. As people are susceptible to multiple infections over a lifetime, each influenza exposure shapes future immune responses to infections and vaccinations. Unfortunately, vaccines are not developed with the human influenza history in mind.

Methods: Using ferrets, the immune responses of preimmune ferrets to influenza vaccination and challenge were investigated. To establish preimmunity, adult ferrets were infected with a sublethal dose of a historical seasonal H1N1 virus. Following recovery, ferrets were vaccinated with the Sanofi QIV split virion vaccine. To evaluate protection, the ferrets were challenged with A/California/07/2009 (Cal/09), a currently circulating virus and one of the components of the QIV vaccine. Following challenge, ferrets were monitored for signs of clinical disease indicated by weight loss, fever, and lethargy.

Results: Preimmune-vaccinated ferrets lost minimal weight and did not experience a temperature increase. Hemagglutination inhibition assays showed significant, sustained increases in antibody titers in preimmune ferrets post-vaccination for antigens in the vaccine compared to titers from naïve-vaccinated ferrets. Furthermore, Cal/09 hemagglutinin antibodies were present at 7 days post-vaccination in preimmune ferrets and absent in the control naïve-vaccinated group. This indicates that animals with an immune background were able to generate vaccine-specific antibodies more quickly. Investigation of the immunoglobulin isotype profiles showed higher levels of virus-specific antibodies of the IgG isotype in the serum of the preimmune-vaccinated ferrets suggesting maturity in antibody-producing B cells.

Conclusions: Together, results showed that preimmune animals had greater responses to vaccination and were more protected during challenge. The early generation of antibodies toward an antigenically distinct virus and the predominant IgG virus-specific antibodies in

circulation suggests plasticity in existing memory B cell clones. Understanding mechanisms of vaccination responses may help design the next generation of vaccines that incorporate both influenza history and immunogenicity.

Poster 15. HIT OR MISS? COMPARISON OF *NEISSERIA GONORRHOEAE* DETECTION LIMITS OF AUTOMATED MOLECULAR METHODS USED ACROSS NOVA SCOTIA

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Introduction: Testing for *Neisseria gonorrhoeae* (GC) is often performed concurrently with *Chlamydia trachomatis* (CT). Due to the low prevalence of GC in Nova Scotia, confirmatory testing is reflexively performed following an initial positive (or indeterminate) GC result. Given the different commercial assays are used for these purposes in NS, the analytical sensitivity of methods used for GC testing was assessed.

Methods: Panels were sent to each NS laboratory performing CT/GC testing consisting of 10-fold serial dilutions of GC, with the final dilution in the recommended buffers for each method. GC screening methods included the Hologic Panther, BD Viper, BD Max, and Roche 4800 systems. GC confirmatory testing was evaluated on the Hologic Panther system, BD Max, or Cepheid Xpert. To assess analytical specificity, non-GC strains of *N. meningitidis* (serotypes B and C), *N. lactamica*, *N. cineria*, *N. sicca*, and *N. subflava* were also tested at high concentrations (>10^7 CFU/ml).

Results: In the specificity analyses, the BD Viper was the only assay that showed cross reactivity (with *N. lactamica*). In the analytical sensitivity analyses, the Hologic Panther and BD Viper systems were the most sensitive screening methods for GC with LoD of 11 $\pm$ 1 CFU/ml, followed by the BD Max at 27 $\pm$ 4, and the least sensitive method was the Roche 4800 at 295 $\pm$ 37 CFU/ml. GC confirmation on the Hologic Panther had equivalent sensitivity to the primary testing method, whereas testing algorithms using BD Max or Xpert for GC confirmation were less sensitive than their screening method at 27 $\pm$ 4 and 31 $\pm$ 4 CFU/ml, respectively.

Conclusions: The most sensitive methods for GC detection and confirmation were the Hologic Panther assays. Given the lower sensitivity of other methods used in Nova Scotia for GC screening and confirmation, testing algorithms may need to be revised.

Poster 16. SUSCEPTIBILITIES OF INVASIVE *NEISSERIA MENINGITIDIS* STRAINS TO AGENTS USED FOR PROPHYLAXIS: A RETROSPECTIVE SURVEY OF NOVA SCOTIA CASES, 2004-2018

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Affiliation: [1.] National Microbiology Laboratory (PHAC), Winnipeg, MB, Canada; [2.] Provincial Public Health Laboratory Network, Halifax, NS, [3.] Department of Pathology, Dalhousie University, Halifax, NS

Introduction: Antimicrobial agents may be used for chemoprophylaxis of contacts of patients with invasive infection with *Neisseria meningitidis*, in the absence of cultures or susceptibility results of the strain. We tested the susceptibilities of invasive strains of *N. meningitidis* to determine the resistance rates to agents commonly used for prophylactic treatment, and to penicillin.

Methods: Fifty strains of *N. meningitidis* isolated from sites that might prompt chemoprophylaxis (25 blood, 20 CSF, 2 conjunctiva, 1 throat, 2 not recorded) between 2004 and 2018 from individual patients (age range 3 months to 95 years) in our province were included. Minimal inhibitory concentrations were determined to rifampin, azithromycin, trimethoprim-sulfamethoxazole, ciprofloxacin, minocycline and penicillin G, using a diffusion gradient strip on Mueller Hinton agar with 5% sheep blood in 5% CO_2 for 20-24 hours. Results were interpreted using the CLSI M100 S28 document. Isolates were serotyped and subtyped.

Results: All isolates were susceptible to rifampin, azithromycin, ciprofloxacin, and minocycline. For trimethoprim sulfamethoxazole, 13 isolates were resistant and 1 intermediate. None of the isolates were resistant to penicillin but 13 were intermediate. One isolate was intermediate to penicillin and resistant to trimethoprim-sulfamethoxazole. There was a trend toward increasing MIC for penicillin G over the time period, but there were no trends identified for the other agents. Group B was the commonest serogroup (31 isolates), there were 9 group Y, 6 group C and 4 group W.

Conclusions: Resistance has not emerged to rifampin, azithromycin, ciprofloxacin, and minocycline locally. Trimethoprim sulfamethoxazole should not be used for chemoprophylaxis of *Neisseria meningitidis* infection in Nova Scotia.

Poster 17. COMPARISON OF HERPES SIMPLEX THE AUTOMATED PANTHER AND VIPER SYSTEMS

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Introduction: Two Health Canada approved assays for detection and differentiation of HSV-1 and HSV-2 were compared retrospectively and prospectively; the BD Probetec HSV 1 & 2 Qx assay on the Viper XTR, and the Aptima HSV 1 & 2 assay on the Hologic Panther. The Aptima assay failed to detect HSV in specimens with low viral loads, resulting in reduced sensitivity for HSV-1 of 85.0% (34/40) and 95.8% (23/24) for HSV-2.

Methods: As recommended by the manufacturers, the Aptima assay was performed on a Panther system, and the BD Probetec assay was performed on a Viper instrument. Analytical sensitivity and specificity were assessed using 10-fold serial dilution of viruses in viral transport media (VTM), and nucleic acids extracted concentrated from other viruses including all members of the Herpesviridae family. The clinical sensitivity and specificity were assessed prospectively using 158 swabs from oral and anogenital sites collected in VTM. Discrepant results were resolved with real-time PCR using the RealStar HSV 1-2 assay (Altona Diagnostics).

Results: Both the Aptima and Viper assays showed excellent clinical and analytical specificity, without any false positive reactions. However, the Aptima HSV assay failed to detect HSV in specimens with low viral loads, resulting in reduced sensitivity for HSV-1 of 85.0% (34/40) and 95.8% (23/24) for HSV-2. The analytical analyses coincided with reduced sensitivity of approximately 10-fold for both HSV-1 and HSV-2 for Aptima compared to the Viper Probetec assay**.**

Conclusions: This study demonstrated that detection of HSV mRNA using the Aptima HSV assay was less sensitive than HSV DNA detection through SDA technology on the Viper system. It is unclear whether this difference is attributed to the methodology itself, or limitations of mRNA-based detection for the diagnosis of infection with DNA viruses like HSV.

Poster 18. EVALUATION OF THE THERAPEUTIC POTENTIAL OF ANTIBODY AND T CELL TARGETED IMMUNE RESPONSES TOWARDS RSV SMALL HYDROPHOBIC PROTEIN

Authors: H. Torrey[1], G. Weir[1], V. Kaliaperumal[1], A.R. Falsey [2], E.E. Walsh[2], J.M. Langley[3], B. Schepens[4], X. Saelens[4], M. Stanford[1]

Affiliation: [1] IMV Inc., Dartmouth NS, [2] University of Rochester NY, USA, [3] CCfV, Halifax NS, [4] VIB, Ghent Belgium.

Introduction: Vaccines targeting the G or F protein currently predominate clinical respiratory syncytial virus (RSV) vaccine development. The small hydrophobic (SH) protein of RSV is poorly accessible within the virion but is highly expressed on the surface of infected cells, making it a unique vaccine target. Clinical evaluation of a novel vaccine candidate containing a peptide from the ectodomain of SH RSV strain A (DPX-RSV(A)) as an antigen target was conducted (NCT02472548). Immune responses of DPX-RSV(A) vaccine recipients was compared to the immune responses in older adults with natural RSV infection.

Methods: Paired serum samples obtained from older adults with symptomatic confirmed RSV were tested for anti-SH(A) IgG titres by ELISA. Antibody binding was evaluated *in vitro* using HEK293T cells expressing SH protein or infected with RSV. Subsequent phagocytosis of these cells was tested by adding macrophages to these cultures. Samples from DPX-RSV(A) vaccinated subjects were also evaluated for binding *in vitro*, and antigen-specific antibody isotypes and T cell response were determined by flow cytometry and IFN-γ ELISPOT, respectively.

Results: Anti-SH(A) titres were detected in 16 convalescent serum samples from RSV-infected adults, 8 of which were also positive in corresponding acute sample. Sero-response did not correlate with clinical variables but was more likely to occur in subjects with detectable anti-SH(A) at acute (p=0.13). Functional assays were performed on 20 pairs. Phagocytosis of SH expressing cells by macrophages was more pronounced in the presence of convalescent sera. Similar functional results were observed in serum of subjects vaccinated with DPX-RSV(A) and who developed anti-S_H(A) titres. In 4 out of 20 subjects vaccinated with DPX-RSV(A), antigen-specific T cell responses were detected in PBMC samples measured by IFN-γ ELISPOT.

Conclusions: Natural RSV infection and vaccination with DPX-RSV(A) induce antibodies towards SH protein that bind the viral protein and which may induce phagocytosis of infected cells. DPX-RSV(A) also induced robust $CD4^+$ T cell responses towards SH. This data further validates SH as a unique target for vaccine development to RSV and supports its relevance to clinical infection in humans.

Poster 19. EFFECT OF COMPOUND 21, A SELECTIVE ANGIOTENSIN II TYPE 2 RECEPTOR AGONIST, IN AN ABDOMINAL ADHESION MURINE MODEL

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Introduction: Abdominal adhesions are fibrous bands that form in response to surgical trauma which connect visceral and/or peritoneal surfaces and can lead to long-term complications. This study uses a murine model of abdominal adhesions to determine the anti-fibrotic effect of a novel selective angiotensin II type 2 receptor agonist, compound 21 (C21), in reducing abdominal adhesion formation.

Methods: Laparotomy was performed on female BALB/c mice and cecum and overlying parietal peritoneum was abraded with sandpaper. Mice were divided into systemic (oral gavage) or local (intraperitoneal injection) groups and treated with C21 (10 μg/kg) or saline (vehicle) daily for 7 days. Mice were sacrificed 8 days post-surgery, adhesions were graded by a blinded observer, and peritoneal fluid was obtained for TGFβ quantification by ELISA. Laparotomy incisions were excised for CD31, CD68, and αSMA immunostaining, and picrosirius red staining. To study in vitro effects, parietal peritoneal fibroblasts and visceral mesothelial cells were isolated and scratch wound assays performed using C21 (10 μM), angiotensin II (AngII, 1 μM), or both.

Results: Systemic and local administration of C21 reduced the formation of abdominal adhesions in vivo. TGFβ in peritoneal fluid was reduced in C21 treated mice. Histological analysis of surgical incisions revealed no difference in the number of CD31+ vessels or CD68+ cells, while αSMA expression was reduced in C21-treated animals. Picrosirius red revealed no difference in collagen I/III distribution, total collagen density, and dermis thickeness in laparotomy scars between control and C21-treated animals. Migration of parietal peritoneal fibroblasts and visceral mesothelial cells in vitro was reduced with C21 compared to control or AngII.

Conclusions: C21 reduced or completely prevented adhesion formation both with local and systemic adminstration. These findings may be attributed to decreased levels of pro-fibrotic TGFβ in vivo and decreased cell migration of parietal peritoneal fibroblasts and visceral mesothelial cell migration in the presence of C21. Importantly, C21 did not have histologically quantifiable effects on laparotomy wounds. This study suggests that C21 could reduce abdominal adhesions without impeding laparotomy healing.

Poster 20. CHARACTERIZING THE ROLE OF LY49 RECEPTORS IN NATURAL KILLER CELL ADAPTIVE IMMUNOLOGICAL MEMORY

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Introduction: Immunological memory is a hallmark of the adaptive immune system. However, recent evidence identified that natural killer (NK) cells, a component of the innate immune system, also mediate antigen-specific memory responses. Previous studies in our lab identified the NK cell receptors, Ly49C or Ly49I, as mediators of NK adaptive memory through their interaction with the MHC-I ligands H-2K^{b} and H-2D^{b}. Here we investigate whether adaptive NK memory formation is limited to Ly49 C/I or if other Ly49s are also capable of mediating antigen-specific NK memory responses in the presence of their specific MHC-I ligands. The results of this study will provide us with a better understanding of the mechanisms behind the adaptive NK memory responses, thereby providing the opportunity to exploit NK memory for use in vaccine development and cancer immunotherapy.

Methods: A mouse ear swelling contact hypersensitivity assay (CHS) was used to test the role of Ly49G receptor activity in adaptive NK memory. Mice lacking T and B lymphocytes (Rag^{KO}) and Ly49G receptors and congenic for MHC-I haplotype H-2^{d} (Rag^{KO}Ly49G^{KO} H-2^{d} mice) were used. A CHS assay was performed by sensitizing mice with chemical hapten 2, 4 dinitrofluorobenzene (DNFB) in a shaved region of abdomen then challenging one ear of the mouse with DNFB after five days. Memory responses were analyzed by recording the ear swelling difference between challenged ear and control ear. To test the ability of Ly49C/I to mediate adaptive NK memory in Rag^{KO} mice congenic for MHC-I H-2^{d} haplotype, the DNFB-induced CHS assay was performed following antibody-mediated depletion of NK cells expressing Ly49C/I receptors.

Results: Mice lacking Ly49G receptors showed no difference in ear swelling response to DNFB compared to controls. However, ear swelling responses to DNFB was significantly reduced in mice depleted of Ly49C/I expressing NK cells.

Conclusions: Overall, our findings show that Ly49C/I can mediate adaptive NK memory by interacting with MHC-I ligands H-2D^{d}, H-2L^{d} and H-2K^{d}, thus illustrating a critical role of Ly49C/I receptor in adaptive NK memory. The presence of memory in mice lacking Ly49G receptors suggests that NK memory may be intrinsic to select Ly49 receptors, such as Ly49C/I. Thus, further studies are needed to define Ly49 receptors roles in NK memory responses.

Poster 21. A RETROSPECTIVE EVALUATION OF A PHARMACIST-LED ANTIMICROBIAL STEWARDSHIP SERVICE IN A PEDIATRIC EMERGENCY DEPARTMENT

Authors: K MacMillan[1,2], E Black[1,2], E Fitzpatrick[1,2], K F Hurley[1,2], S MacPhee[1,2], K Matheson[1,3], M MacInnis[1,2].

Affiliation: [1]Dalhousie University [2]IWK Health Centre, [3]Nova Scotia Health Authority

Introduction: A pharmacist-led antimicrobial stewardship (AMS) service for patients discharged from the pediatric emergency department (PED) was implemented at the IWK Health Centre in Halifax, Canada. The objectives of this study were to evaluate the impact of this service on the rate of return visits to the PED, appropriateness of antimicrobial therapy, and time to notification.

Methods: This study was completed as a retrospective chart review of pediatric patients discharged from the PED 6 months before and after implementation of the pharmacist-led AMS service. Data was extracted from electronic medical records. Data were reported descriptively and compared using a two-sided chi-square test and ordinal logistic regression.

Results: This study included 1070 patient encounters pre-implementation and 1040 patient encounters post-implementation. The rate of return visits to the PED within 96 hours was 12.0% (129/1070) pre-implementation vs 10.0% (100/1049) post-implementation (p = 0.07). The rate of return visits or hospitalization at 30 days was 22.1% (237/1070) pre-implementation compared to 19.9% (207/1040) in the post-implementation phase (p = 0.21). Inappropriate antimicrobial therapy was identified more often in the pre-implementation phase (7.0%, 68/975) vs the post-implementation phase (5.0%, 46/952), p = 0.047. Time to notification within the first day after discharge occurred more frequently in the post-implementation phase (53.3%, 80/150) as compared to the pre-implementation phase (40.3%, 52/129, p = 0.0298).

Conclusions: Although this pharmacist-led AMS service did not significantly affect the rate of return visits or hospitalization, it may have led to more judicious use of antimicrobial agents and faster time to notification.

Poster 22. THE EFFECTS OF AID GENE KNOCKOUT ON *CHLAMYDIA MURIDARIUM* IMMUNOPATHOLOGY

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Introduction: *Chlamydia trachomatis* (*Ct*) is a sexually transmitted infection that can significantly impact women's health due to long-term complications, such as pelvic inflammatory disease and tubal factor infertility, which are associated with persistent infections. Previous research has demonstrated a conflicting role for antibodies produced during *Ct* infections; antibodies can provide protection during re-infection, but there are also reports that antibodies can cross-react with host tissues, thus intensifying tissue damage.

Methods: In order to more clearly elucidate the role that high-affinity antibodies can have during *Ct* infection responses, an AID (activation-induced cytidine deaminase) gene knockout murine model was used. Both AID KO (knockout) mice and CD45.1 WT (wild-type) mice were infected 5 times with low doses of *Chlamydia muridarium* (*C.m*.), then re-challenged with a single high dose of *C.m.* following clearance of the initial infection.

Results: A two-way ANOVA of quantitative PCR results did not suggest that there were differences in bacterial burden levels between the groups. Although previous studies have reported that IgM, but not IgG, is produced in AIDKO mice, ELISA assays revealed that the *C.m*. infected AIDKO group produced significantly more IgG than the WT group in response to heat killed *C.m*., as well as to individual antigens that were or were not associated with tissue pathology. ELISA assays also revealed that there were differences in cytokine levels between the AIDKO and WT group, as the mean levels of interferon-gamma and interleukin-10 were higher in the AIDKO groups. Furthermore, visual investigation of isolated genital tracts demonstrated that although both groups had *C.m*.-associated oviduct cysts, the gross pathology observed in the AIDKO tracts seemed to have more severe tissue damage overall.

Conclusions: The results suggest that AID activity predominantly promotes a protective response during *Chlamydia.* infections, however it is unclear why *C.m*. infections elicit such high levels of IgG in a model that produces no IgG during non-chlamydial challenges. Further investigation is required to determine the mechanism of this protection, as well as to clarify the complex humoral response during *Chlamydia* infections.

Poster 23. IMMUNIZATION STRESS RELATED RESPONSES (ISRRs)

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Introduction: Vaccines and Immunizations are now well recognized as crucial to human health on a global scale. Maintaining the effectiveness of immunization programs worldwide requires maintaining public trust in the safety of immunization injections. Immunization Stress Related Responses (ISRRs) are a collection of biopsychosocial responses that individuals and groups may have before, during and after immunization. Bettering front-line immunizations workers understanding and ability to deal with these reactions can improve immunization safety and bolster public trust in immunization programs worldwide.

Methods: Education and presentation materials for front-line immunization workers were developed based on the WHO guidelines “Immunization Stress Related Responses- A manual for program managers and health professionals to prevent, identify and respond to stress-related responses following immunization”.

Results: The presentation and case studies were well received when they were presented in Jakarta, Indonesia as part of the Regional Intercountry AEFI SEAR meeting. Amongst the AEFI reported were two ISRRs that resulted in hospitalization. More information and education on how ISRR clusters impact immunization programs, the biopsychosocial model, needle fear and long-term health outcomes, and better communication with the public and the media about ISRRs, were all requested by the pilot audience at that presentation.

Conclusions: ISRRs are a regular occurrence globally. As such, front-line immunization workers are often eager to better their understanding of how to prevent, recognize and effectively deal with ISRRs. Similar training modules are intended to be available globally through the WHO, as well as locally in NS and across Canada. Providing educational resources and presentations for this purpose will ideally improve immunization safety and public trust in immunizations.

Poster 24. OPTIMIZNG TREATMENT OF BLOODSTREAM INFECTIONS: IMPACT OF ANTIMICROBIAL STEWARDSHIP INTERVENTION FOLLOWING FINAL SUSCEPTIBILITY REPORT

Authors: T Canning, V Murphy, R Davidson, P Bonnar

Affiliation: Dalhousie University & Nova Scotia Health Authority

Introduction: Inappropriate use of antibiotics poses a number of risks such as increased risk of side effects and an increased chance of bacterial resistance. The impact of an Antimicrobial Stewardship (AMS) program in Nova Scotia is still unknown but it has the potential to allow for antimicrobial optimization. The objective of our study was to determine if reviewing susceptibility results for blood stream infections (BSI) and providing feedback to prescribers optimizes antimicrobial therapy & to assess the frequency of accepted interventions suggested by the AMS team.

Methods: 174 reports of positive BSI were reviewed by the AMS team and recommendations were made to the care team regarding treatment when therapy could be optimized. A retrospective chart review was then conducted by reviewing the health records of 22 patients who required AMS intervention. Charts were reviewed to monitor the acceptance of recommendations, duration of final drug therapy and the total number of days antibiotics were prescribed. Exclusions were patients with febrile neutropenia, cystic fibrosis, if the infectious disease physicians were already consulted or if current therapy required no intervention. Results were summarized descriptively.

Results: 13% of patients required AMS intervention for therapy optimization. Interventions included switching from an oral medication to an IV medication, broadening therapy, increasing dose, and the majority (73%) involved narrowing of therapy. The overall acceptance of interventions was 64% by the patient's care team. Median duration of antibiotic use was less when interventions were accepted. When AMS intervention was accepted antibiotic use was less variable and 57% of patients received cefazolin as their final drug therapy.

Conclusions: Antimicrobials are frequently used in the hospital setting for BSI. AMS optimized antimicrobial therapy in a small percentage of BSIs, 64% of which were implemented by the care team. Narrowing of antimicrobial therapy was the most frequent intervention and patients tended to have a shorter duration of antibiotic therapy when recommendations were accepted. Areas identified for quality improvement include investigating strategies to increase acceptance of recommendations and to develop an efficient process for BSI management.

Oral Presentation Abstracts

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

Oral Presentation 1. IS STREPTOCOCCUS PNEUMONIAE SEROTYPE 3 MASKING PCV13-MEDIATED HERD IMMUNITY IN ADULTS HOSPTALIZED WITH COMMUNITY ACQUIRED PNEUMONIA?

Authors: J J LeBlanc [1*], M ElSherif [1], L Ye [1], D MacKinnon-Cameron [1], A Ambrose [1], T F Hatchett [1], I Martin, M K Andrew [2], G Boivin [3], W Bowie [4], K Green [5], J Johnstone [6], M Loeb [6], A McCarthy [7], A McGeer [8], M Semret [8], S Trottier [3], L Valiquette [9], D Webster [10], S A McNeil [1], on behalf of the Serious Outcomes Surveillance (SOS) Network of the Canadian Immunization Research Network (CIRN).

Affiliation: [1]Canadian Center for Vaccinology (CCfV), IWK Health Centre, Nova Scotia Health Authority (NSHA), and Dalhousie University, Halifax, Nova Scotia (NS); [2]National Microbiology Laboratory (NML), Winnipeg, MB; [3]Centre Hospitalier Universitaire de Québec, Québec, Québec (QC); [4]Vancouver General Hospital, and University of British Columbia, Vancouver, BC; [5]Mount Sinai Hospital, Toronto, ON; [6]McMaster University, Hamilton, ON; [7]Ottawa Hospital General Campus, Ottawa, ON; [8]McGill University Health Centre, Montreal, QC; [9]Centre Intégré Universitaire de Santé et de Services Sociaux de l'Estrie – Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, QC; [10]Saint John Regional Hospital, St. John, NB.

Introduction: The 13-valent pneumococcal conjugate vaccine (PCV13) was recently shown to be effective against PCV13-type invasive pneumococcal disease (IPD) and pneumococcal community acquired pneumonia (CAP-Spn) in healthy adults aged ≥65 years, prompting many countries to re-assess adult immunization. In Canada, the potential benefits of adult PCV13 immunization were unclear given anticipated herd immunity from PCV13 childhood immunization introduced since 2010. This study describes the serotype distribution and clinical outcomes of Canadian adults aged ≥16 years, who were hospitalized with CAP-Spn and IPD from 2010 to 2015.

Methods: Active surveillance for CAP and IPD was performed in adult hospitals across five Canadian provinces. IPD was identified when Streptococcus pneumoniae was isolated from sterile sites. Bacteremic and non-bacteremic CAP-Spn were identified using blood culture, and sputum culture or PCV13-specific urine antigen detection (UAD-PCV13), respectively. Serotype was assigned using Quellung reaction, PCR, or UAD-PCV13.

Results: Of 6687 CAP cases where a test was performed, S. pneumoniae positivity decreased from 15.9% in 2011 to 8.8% in 2014, but increased to 12.9% in 2015. CAP-Spn attributed to PCV13 serotypes followed a similar trend, dropping from 8.3% in 2010 to 4.6% in 2014, but increasing to 6.3% in 2015. The decline was primarily attributed to serotypes 7F and 19A, and the proportional increase to serotype 3. Similar trends were noted for bacteremic and non-bacteremic CAP-Spn. Serious outcomes such as 30-day mortality, intensive care unit admission, and requirement for mechanical ventilation were prominent in CAP-Spn and IPD cases, but remained unchanged over the study years.

Conclusions: Herd immunity afforded primarily by serotypes 7F and 19A appears to be partly masked by a concomitant proportional increase of serotype 3. Despite evidence of herd immunity, these PCV13 serotypes remain persistent in Canadian adults hospitalized with CAP-Spn, and represent between 5 to 10% of all CAP in this patient population. For now, our data supports the recent interim recommendation by NACI for the use of PCV13 in adults aged ≥65 years, but it is unclear whether herd immunity is complete. Ongoing surveillance will be required.

Oral Presentation 2. COMPOSITION OF KSHV RIBONUCLEOPROTEIN COMPLEXES

Authors: E S Pringle [1], C McCormick [1,2,3]

Affiliation: [1]Department of Microbiology & Immunology, Dalhousie University, [2]Beatrice Hunter Cancer Research Institute, [3]Canadian Center for Vaccinology

Not published by request.

Oral Presentation 3. DEVOLOPMENT OF QUALITY INDICATORS TO EVALUATE APPROPRAITE EMPIRIC ANTIMICROBIAL USE IN PEDIATRIC PATIENTS

Authors: H MacKinnon [1,2], K Slayter [2,3], J Comeau [2,3], M Science [4], K Timberlake [4], E Black [1,2]

Affiliation: [1]College of Pharmacy, Dalhousie University**,** [2]IWK Health Centre**,** [3]Department of Medicine, Dalhousie University**,** and [4]The Hospital for Sick Children

Introduction: Definitions of "appropriate" antimicrobial use are inconsistently reported. The primary objective of this study was to obtain consensus on quality indicators that describes appropriate empiric antimicrobial use for management of infectious syndromes in hospitalized pediatric patients.

Methods: This study was completed using the Delphi technique, which consisted of a series of questionnaires, designed to obtain a consensus from an expert panel. A panel of pediatric infectious disease physicians and pharmacists in North America were invited to participate. Panelists were asked to rate indicators on a 9-point Likert scale considering the following criteria; "The importance of each item in determining appropriateness considering benefit or harm at the individual or population level". Consensus was defined as ≥ 75% agreement and a median score of ≥ 7. In the final round, panelists were asked to rank the top 5 indicators that had achieved agreement in order of importance.

Results: Four rounds of questionnaires were distributed to the expert panel between July 2018 and December 2018. Twelve panelists completed the first round of the survey, 10 panelists completed the second and third rounds, and 11 panelists completed the fourth round. After three rounds, 24/25 quality indicators initially proposed and 3/6 quality indicators suggested by panelists reached consensus. The most highly ranked indicator was "empiric choice of antimicrobial agents for pediatric patients should be active against the most likely causative pathogens".

Conclusions: This study achieved consensus on quality indicators for appropriate empiric antimicrobial use for management of infectious syndromes in hospitalized pediatric patients.

Oral Presentation 4. ATTITUDES TOWARD INFLUENZA VACCINATION DURING 'WAIT TIMES' IN THE EMERGENCY DEPARTEMENT

Authors: N Ozog, A Steenbeek, J Curran, N Kelly

Affiliation: Dalhousie University

Introduction: Influenza is a burdensome and preventable infectious disease. Lack of time was the reported reason 15% of Canadians did not receive their influenza vaccine; this presents an opportunity to combine the task of influenza prevention with the logistical issue of another health system challenge: escalating emergency department (ED) wait times. At the Queen Elizabeth II Health Sciences Centre (QEII) in Halifax, NS, average wait time is 4.6 hours. Offering the influenza vaccine during this time could increase access to health services, and ultimately, improve vaccination rates.

Methods: This cross-sectional study aimed to gauge public interest, health care provider (HCP) support, barriers and facilitators to influenza vaccine availability at the QEII ED. Data was collected via anonymous questionnaires between October 28 and December 14, 2018. Client participants were a convenience sample of low-acuity adult QEII ED clients (n=150). HCP participants were a convenience sample of QEII ED nurses, physicians and paramedics (n=82).

Results: Of the unvaccinated clients, 34.6% were willing to be vaccinated in the ED. Clients vaccinated in 2017/18 were five times more likely to be willing to receive ED vaccination ($p<0.0001$). The top factors associated with 2017/18 vaccination were trust in vaccine information, immunity preferences, and beliefs about efficacy ($p<0.0001$). 82% of HCPs support ED vaccination if time and resources were unlimited, while 58% remain supportive in light of current QEII ED time and resources. Most HCPs preferred screening at triage (56.8%) and ordering by medical directive (74.1%). The high risk groups with the lowest HCP endorsement of vaccination were people involved in poultry culling (75.6%), pregnant people (81.7%) and children 6-59 months (84.1%).

Conclusions: QEII clients and HCPs are supportive of ED influenza vaccination. However, there are knowledge gaps among both groups that would need to be addressed to effectively launch such a program.

Oral Presentation 5. TLR2 EXPRESSING BONE MARROW DERIVED LEUKOCYTES INDUCE T_H17 RESPONSE IN *CHLAMYDIA* GENITAL INFECTION

Authors: A Mayavannan [1,2], E Shantz [1,2], A Edgar [1], R Clarke [2], G Rooke [1], I Haidl [1], J Marshall [1], J Wang [1,2]

Affiliation: [1] Dalhousie University, Halifax, Nova Scotia, Canada, [2] Canadian Center for Vaccinology, IWK Health Centre, Nova Scotia, Canada.

Introduction: *Chlamydia trachomatis* (*Ct*) is the most common bacterial STI and causes severe reproductive tissue damage in women. Unresolved chronic infection in mucosa epithelium and/or uncontrolled immune responses may contribute to *Ct*-induced tissue pathology. TLR2 is a pathogen-sensing molecule expressed broadly by epithelium and immune cells, yet, its role in *Ct* pathogenesis remains controversial.

Methods & Results: To this end, we compared the course of infection in $TLR2^{+/+}$ and $TLR2^{-/-}$ mice following intravaginal inoculation of *Chlamydia muridarum* (*Cm*). Compared to $TLR2^{+/+}$ mice, $TLR2^{-/-}$ mice had significantly increased vaginal bacterial shedding and markedly increased tissue pathology at day 75 post-infection although they seemingly had reduced tissue pathology at day 55. In parallel with the dynamic change in tissue pathology, $TLR2^{-/-}$ mice also displayed a time-dependent T helper 2 (T_H2) immune response, indicated by the levels of IL-13 production from splenocytes upon *Cm* antigen re-stimulation. However, $TLR2^{-/-}$ mice showed consistently reduced IL-17A production, indicating a critical role of TLR2 in developing T_H17 response. Bone marrow chimeric mice were generated to further define the contribution of TLR2-expressing immune cells and TLR2-expressing epithelium. Notably, IL-17A was only detected in mice having TLR2-expressing bone marrow-derived immune cells.

Conclusions: Collectively, our data demonstrate a critical role of TLR2 in host defence against *Chlamydia* infection and the development of *Chlamydia*-induced tissue pathology. Our data also highlights an essential role of TLR2-expressing bone marrow-derived leukocytes in driving the development of T_H17 response, which may be required for controlling pathological T_H2 response and oviduct pathology in later stages of *Chlamydia* genital infection.

Oral Presentation 6. HOST-TARGETED ANTIVIRALS BLOCK INFLUENZA VIRUS REPLICATION

Authors: P Slaine [1], M Kleer [1], M Roberge [2], A Balgi [2], I Haidl [1], N Smith [1], D Khaperskyy [1], C McCormick [1]

Affiliation: [1]Department of Microbiology & Immunology, Dalhousie University, [2]Department of Biochemistry and Molecular Biology, University of British Columbia

Not published by request.

Oral Presentation 7. HEALTHCARE PROVIDER UNDERSTANDING OF VACCINE PRODUCT MONOGRAPHS

Authors: K Weagle, T Manca, M Kervin, N MacDonald, K Top, J Graham

Affiliation: Dalhousie University, Halifax, NS, Canada

Introduction: Gaps in scientific evidence and healthcare provider (HCP) knowledge may contribute to distrust in vaccine safety and effectiveness. During a consensus workshop to develop evidence-based Product Monograph (PM) language for vaccine use in pregnancy, we discovered that HCPs were unaware of regulatory requirements including technical limitations/restrictions governing the purpose, content and language of PMs. The aim of this study was to evaluate Canadian HCPs' understanding of the evidence-base and purpose of PMs.

Methods: This was a cross-sectional study of Canadian HCPs. We invited HCPs to complete a 30-item online survey to evaluate the revised PM language developed during the consensus workshop. Our survey included questions on trust in various information sources, PM use, and the extent of agreement on statements about the purpose and types of information in PMs. The survey was distributed across Canada via health professional organizations in English and French using Opinio software.

Results: 449 HCPs across urban and rural Canada responded, including family physicians, obstetricians, midwives, nurses, and pharmacists. 54% of respondents strongly/somewhat agreed that the purpose of PMs is to provide information on the vaccine-preventable disease; 80% agreed that PMs provide recommendations for vaccine use; 44% said that PMs included all relevant post-marketing efficacy and safety data; 38% said that PM data was up-to-date; 38% agreed that PMs contained information similar to public health recommendations when these statements are not true of PMs. 24-30% of responses pertaining to evidence, and 2-24% of responses pertaining to purpose were neutral. Further analysis is ongoing.

Conclusions: Respondents frequently agreed that PMs included information such as post-marketing data that is in fact not required by PM guidelines. Results suggest a lack of knowledge about the purpose and evidence contained in PMs amongst HCPs. These gaps in knowledge may influence vaccine use. The results will inform guidelines for developing PMs that support evidence-based vaccine use among pregnant women.

Oral Presentation 8. NK CELL MEMORY RESPONSE IN CANCER IMMUNOTHERAPY

Authors: D Medina-Luna, G Gamage, M Scur, H Zein, B D Parsons, A P Makrigiannis

Affiliation: Department of Microbiology and Immunology, Dalhousie University, NS

Introduction: Immunological memory has been solely attributed to the adaptive immune system; however, we now know that natural killer (NK) cells also possess an analogous function. It was observed that Rag-1-deficient mice ($Rag^{-/-}$), which lack T and B cells, retain immunological memory mediated by NK cells. Previous work showed that adaptive NK cell responses can protect immunized mice against a tumor challenge. However, it remains unclear how memory NK cells protect the host against tumor development. This project will advance our understanding of anti-cancer immune responses mediated by NK cells, and will test its application in cancer immunotherapy through vaccination.

Methods: $Rag^{-/-}$ mice were immunized with the $HPV16E7_{49-57}$ (RAHNIVYTIF; R9F) peptide, from the human papilloma virus oncogene E7, using the proprietary vaccine formulation DepoVax (DPX), (IMV, Inc., Dartmouth, Canada). Sixteen days after immunization, mice were subcutaneously injected with C3 tumor cells that express the R9F antigen. As a therapeutic approach, a separate group of mice received the DPX-R9F vaccine 2 days post tumor implantation. A control cohort of $Rag^{-/-}$ mice in all experiments received DPX alone. The proportion of mice that developed tumors and the rate of tumor growth were recorded and compared between both groups.

Results: $Rag^{-/-}$ mice vaccinated with DPX-R9F had a better protection against C3 tumor development, as 60% of the mice vaccinated either before or after tumor implantation remained tumor-free in comparison to the control groups, in which all mice developed tumors. Additionally, the growth rate of tumors in $Rag^{-/-}$ mice vaccinated with DPX-R9F was significantly slower that tumors in mice that recieved the empty vaccine formulation.

Conclusions: Our preliminary results suggest that DPX-R9F vaccination induces protection against tumor development in mice in a T cell- and B cell-independent manner. Whether this protection relies only on memory NK cells is still unclear. Future cancer immunotherapies could be improved by priming not only T cells but also NK cells. Considering the natural cytotoxic profile of NK cells and their lack of potential to cause Graft Versus Host diseases, an NK-targeted therapeutic approach may provide better patient outcomes and improve the safety of existing immunotherapies.

Oral Presentation 9. DEFINING MECHANISMS BY WHICH INFLUENZA ALTERS SURFACE EXPRESSION OF MHC-I

Authors: M M A Rahim, E Price, B Chilvers, H Ajami, H Zein, P Slaine, D Medina-Luna, G Seaton, **B D Parsons**, D Khaperskyy, C McCormick, A P Makrigiannis.

Affiliation: Department of Microbiology and Immunology, Dalhousie University, NS

Introduction: Early influenza A virus (IAV) infection of the respiratory epithelium is countered by a variety of innate immune defences. RIG-I detects IAV RNA structures and activates mitochondrial antiviral signalling protein (MAVS) to induce antiviral interferon (IFN) responses. This causes recruitment of immune effector cells, such as natural killer (NK) cells, that recognize and eliminate infected cells. IAV can evade NK antiviral responses by increasing cell surface expression of class I major histocompatibility complex proteins (MHC-I), which impede NK activity through NK inhibitory receptors. Our understanding of how MHC-I is modulated during IAV infection is incomplete; therefore, we investigated the mechanisms by which IAV upregulates MHC-I to evade host responses.

Methods: Human lung A549 and MAVS-mutant A549 cells (A549ΔMAVS) were infected with the mouse-adapted A/Fort Monmouth/1/1947 (FM) IAV or A/Puerto Rico/8/1934 (PR8) or treated with IFNβ, IFNλ1 and IFNλ2 at different durations. Media transfer assays were performed by culturing A549 cells in UV-treated conditioned media (CM) from IAV-infected cells. HLA and IFN levels in IAV-infected and IFN-treated cells were measured by quantitative PCR. We used flow cytometry to measure MHC-I surface expression of cells labelled with anti-HLA-A/B/C, HLA-B, C, and E antibodies.

Results: HLA-A, B and C transcripts and HLA-A/B/C, B, C and E surface expression increased in FM-infection of A549 cells but were mostly absent in A549ΔMAVS cells. By contrast, PR8-infection of MAVS-sufficient A549 cells exhibited increased levels of HLA-C and E transcript, with little to no change in HLA surface expression. A549 cells cultured in UV-treated CM from IAV-infected cells showed an upregulation of HLA levels. Treatment of cells with IFNβ, IFNλ1 and IFNλ2 recapitulated the upregulation of HLAs in A549ΔMAVS.

Conclusions: Our findings show that FM IAV infection upregulates HLAs in a MAVS-dependent manner. This HLA upregulation appears to be mediated directly or indirectly by Type I and III IFNs. The miniscule HLA modulation by PR8 suggests that the ability to circumvent NK immune defenses by IAVs is strain-specific. Together our findings present a potential mechanism by which IAV-infection upregulates MHC-I to inhibit NK cell function.

Oral Presentation 10. INVESTIGATION OF THE INFLUENCE OF HOST IMMUNE HOSTORY ON THE OUTCOME OF INFLUENZA VIRUS VACCINATION IN A PREIMMUNE MOUSE MODEL

Authors: M Francis [1], M King [1], J Marshall [1], C McCormick [1], A Kelvin [1,2,3]

Affiliation: [1] Department of Microbiology and Immunology, Faculty of Medicine, Dalhousie University, Halifax, NS, [2] Department of Pediatrics, Division of Infectious Disease, Faculty of Medicine, Dalhousie University, Halifax, NS, [3] Canadian Center for Vaccinology, IWK Health Centre, Halifax, NS

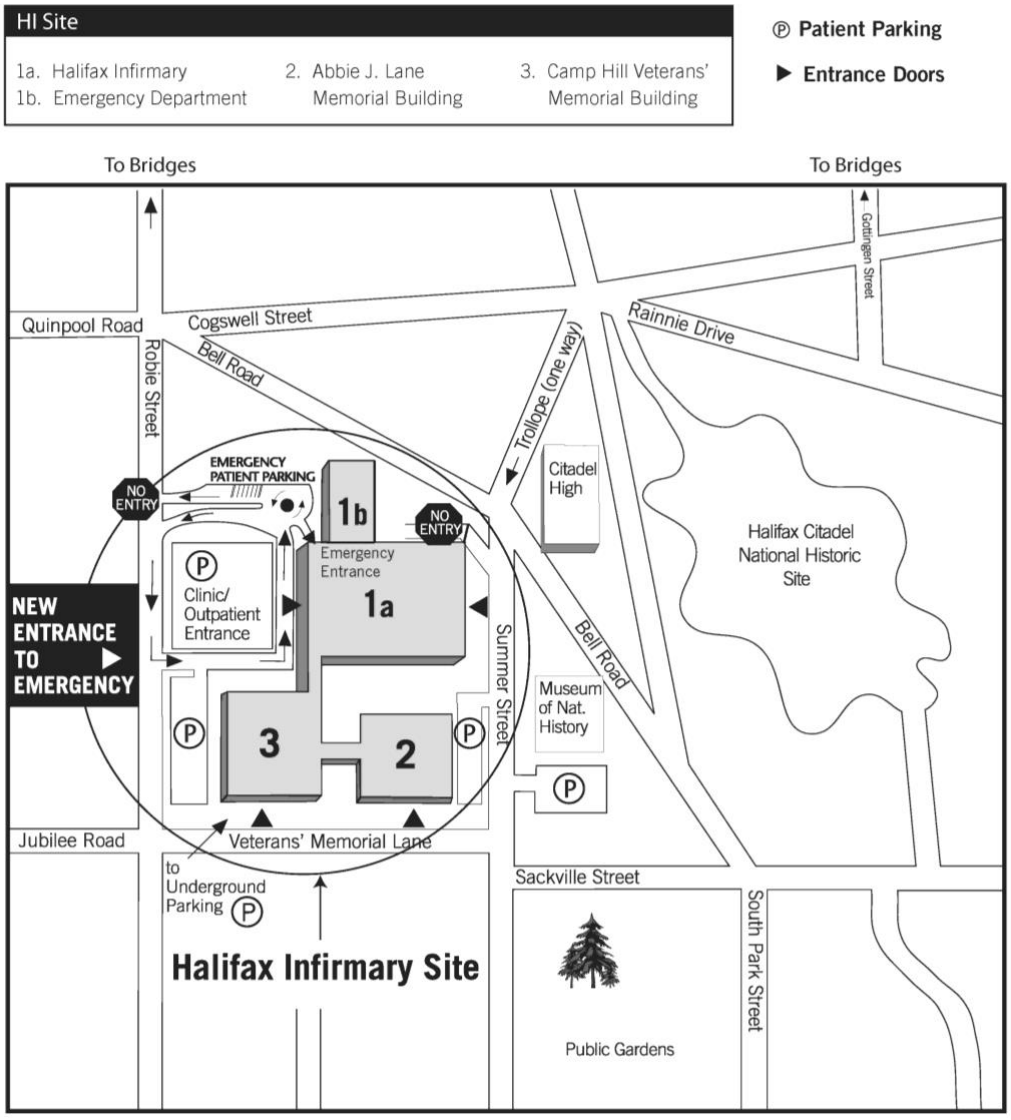
Introduction: Influenza A viruses circulate annually through the human population accumulating genome mutations that affect virus antigenicity. Due to continual antigenic change and virus seasonal cycling, individuals will be exposed to multiple strains of influenza virus over their lifetime, creating an influenza immune history or preimmunity. Despite this, most experimental studies investigating influenza virus immunity or vaccine efficacy utilize naïve hosts. This may not accurately represent the human condition.

Methods: Here we developed a mouse model (C59Bl/6J background) of influenza preimmunity to investigate the effects of vaccination on mice that had previously been exposed to an influenza virus. Mice were infected with a nonlethal dose of A/Brisbane/59/2007 to create a preimmune background. The mice recovered over 60 days to allow for innate immune responses to return to baseline and the development of adaptive memory. Mice were vaccinated with the 2018-2019 Sanofi quadrivalent seasonal influenza vaccine. Following a second recovery period of 45 days, mice were infected with a lethal dose of a pandemic H1N1 2009 virus. Clinical disease (weight loss), viral load, Hemagglutinin Inhibition (HAI) titres, and lung immune responses were assessed.

Results: After vaccination, preimmune mice had statistically higher titres to vaccine antigens compared to naïve vaccinated mice suggesting an immune background increased vaccine promoted immune responses. Control naïve-unvaccinated mice infected with H1N1 2009 had significant weight loss leading to 100% mortality by day 8 post infection. We measured interleukin-6 (IL-6) in the lung as a marker of proinflammatory regulation in all groups. Gene expression analysis revealed marked upregulation of IL-6 and IL-6 inducible genes including STAT3 and SAA3 in the naïve-unvaccinated mice.

Conclusions: Leveraging preimmune animal models of vaccine efficacy is essential for uncovering the immune mechanisms that lead to protection.

QEII Halifax Infirmary Site
(Lecture in Royal Bank Theatre)



Dalhousie University Site
(Presentations held in SUB)