27th Annual Infectious Diseases Research Day

&

14th Annual Canadian Center for Vaccinology Symposium

DALHOUSIE UNIVERSITY
FACULTY OF MEDICINE
Continuing Professional Development

Canadian Center for Vaccinology
Dalhousie University
IWK Health
NS Health

April 26, 2022
Halifax, Nova Scotia

Sponsored by:

Canadian Center for Vaccinology

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

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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:

Planning Committee Members

Karina Top, Chair
Asra'a Abidali
Glenn Patriquin
Jennifer Isenor
Landon Getz
Michael Fleming
Susan Brushett
Yayha Shabi
Allison Young

Welcome to the 27th Annual Infectious Diseases Research Day and 14th Annual CCfV Symposium!

Karina Top, MD, MS, FRCPC
Division of Infectious Diseases, Department of Pediatrics and Community Health & Epidemiology

Welcome to the Infectious Diseases Research Day and CCfV Symposium for 2022. This annual event provides a unique learning opportunity for researchers, trainees, public health professionals, healthcare providers, and community members featuring experienced presenters, and inspired research trainees. Our goal is to highlight Canadian research by established investigators, as well as showcase emerging talent. Our program this year is filled with a variety of presentations and posters themed around various aspects of vaccinology and COVID-19, and the impacts of the global pandemic two years in. We aim to identify research strengths and build new collaborations to extend local research connections.

Feedback and evaluation is important, and **your input is essential for our future planning**. You will receive an email inviting you to take our post-event survey shortly after the conference, and we urge you to give us your feedback to improve this learning event.

Welcome and thank you for joining us!

Scott Halperin MD, FRCPC
Director
Canadian Center for Vaccinology

The Infectious Diseases Research Day/CCfV Symposium is an important annual platform that allows local researchers to present their work and learn about the work of their colleagues. We encourage everyone to take part in this one-day event that will feature interesting topics surrounding infectious diseases. One of the great aspects of this event is that it gives researchers at different stages in their careers the opportunity to learn about the work of their colleagues, and I encourage everyone to make the most of this educational experience.

I would like to offer my sincerest thanks to our planning committee and the financial support from our corporate sponsors. This event would not be possible without the dedicated work and continued support from these individuals.

27th Annual Infectious Diseases Research Day & 14th Annual Canadian Center for Vaccinology Symposium

Schedule of Events

Tuesday, April 26, 2022
8:00am – 4:30pm

Log on at the following link:
https://us02web.zoom.us/j/89218864773?pwd=RndTNTVqM0k4ZFhnNkRMYmQrd3VwUT09

8:00 – 9:00am TJ Marrie Lecture (unaccredited): **Introduction, Dr. Shelly McNeil**

Dr. Angela Rasmussen, *Evolutionarily Happy Ever After: The Future of SARS-CoV-2 and its Hosts*

9:20 – 9:30am Welcome and opening remarks: **Dr. Karina Top, Dr. Scott Halperin, and Dr. Shelly McNeil**

9:30am – 12:35pm Oral Presentations: **Moderated by Drs. Jennifer Isenor and Glenn Patriquin**
Judges: Dr. David Haldane and Dr. Emily Black

9:30am	Melissa Andrew
9:47am	Anima Mayavannan
10:04am	Alexa Davis
10:21am	Daniel Median-Luna
10:38am	Stephana Moss
10:55am	**BREAK**
11:12am	Sarah Kim
11:29am	Beth MacDonald
11:46am	Henrique Pott Junior
12:03pm	Alexa Wilson
12:20pm	Tiffany Fitzpatrick

12:35 – 1:00pm Lunch Break

1:00 – 2:00pm Poster Presentations: (concurrent sessions): **Moderated by Landon Getz**

POSTER PRESENTATIONS	
PhD/Residents/Masters	**Undergraduate Students**
Taylor Caddell	Tyler Sherwood
Fahima Hassan	Nardeen Grace
Yahya Shabi	Estelle Samaraweera
Alina Butova	Trinity Tooley
Gayani Gamage	*Judges: Ian Davis/Paul Bonnar*
Farhan Khan	
Judges: Bob Bortolussi/Glenn Patriquin	
Faculty/Industry (Not judged)	**Research Staff**
Melissa Andrew	Brett Duguay
Sunita Mulpuru	Emily Fitzgerald
Henrique Pott Junior	*Judges: Scott Halperin/Jenn Isenor*
Voica Racovitan/Rachael Stone	
Sharon Oldford	
Ziyad Allehebi/Elizabeth Simms	

2:00 – 3:00pm Presentation: **Introduction, Dr. Scott Halperin**
Dr. Volker Gerdts, *Responding to a global pandemic - lessons learned*

3:00 – 3:15pm Break

3:15 – 3:45pm Presentation: **Introduction, Dr. Glenn Patriquin**
Dr. Jacqueline Gahagan, *Testing Innovation: What we can learn about STBBI testing in the context of COVID*

3:45 – 4:15pm Presentation: **Introduction, Dr. Jenn Isenor**
Dr. Emily Black, *Evaluating antimicrobial use and stewardship in Nova Scotia*

4:15 – 4:30pm Awards ceremony and closing: **Dr. Karina Top**

This program is supported by educational grants from

Sanofi Pasteur, Merck, Pfizer, GSK, Moderna and Gilead

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Speakers

Dr. Angela Rasmussen

Dr. Angela (Angie) Rasmussen, PhD is a virologist at the Vaccine and Infectious Disease Organization (VIDO) at the University of Saskatchewan. Her research focuses on the role of the host response in viral pathogenesis, with a particular interest in emerging viruses that are or have the potential to be major threats to global health.

Dr. Rasmussen graduated from Smith College with a BA in Biological Sciences (2000) and received a MA (2005), MPhil (2006), and PhD (2009) in Microbiology and Immunology from Columbia University. She did her postdoctoral fellowship at the University of Washington She is a member of the WHO Ad Hoc Expert Committee for Preclinical Models of COVID-19 and sits on the Editorial Boards at Vaccine, mSphere, and Cell Reports.

Dr. Rasmussen is a prolific science communicator, as well as a writer for numerous publications including Forbes, the Washington Post, and the New York Times. She is passionate about advocating for equity in biomedical research and public health and that biosecurity and global public health require collaborative international efforts.

Dr. Volker Gerdts

Dr. Volker Gerdts is the Director and CEO of the Vaccine and Infectious Disease Organization (VIDO), located at the University of Saskatchewan in Saskatoon, Canada. He previously served as Associate Director of Research of VIDO from 2007 until 2018. Dr. Gerdts is also a Professor for Veterinary Immunology in the Department of Veterinary Microbiology at the Western College of Veterinary Medicine at the University of Saskatchewan. He received a DVM in 1994 from Hanover Veterinary School and a German PhD equivalent from the Federal Research Institute for Animal Health, Island of Riems and Hanover Veterinary School, Germany in 1997. He has served in various administrative roles and served on various editorial boards and national and international scientific review panels including NIH, CEPI, STAR-IDAZ, CIHR, CFI, NSERC, and the Gairdner Foundation.

Dr. Jacqueline Gahagan

Jacqueline (Jacquie) Gahagan, PhD (medical sociology) joined MSVU as Associate Vice-President, Research on September 1, 2021. Prior to joining MSVU, they were a Full Professor of Health Promotion in the Faculty of Health at Dalhousie University where they taught community health promotion strategies, program planning, and measurement and evaluation courses. Jacquie serves as the Co-Director of the Atlantic Interdisciplinary Research Network for Social and Behavioural Aspects of HIV and HCV (airn.ca), as a Founding Fellow of the MacEachen Institute for Public Policy and Governance and is an Affiliate Scientist with the Nova Scotia Health Authority. Prior to this, Jacquie held a variety of Research Scholar and Research Associate positions with the Jean Monnet European Union Centre of Excellence, the Atlantic Centre of Excellence for Women's Health, the Health Law Institute, the Healthy Populations Institute, the Beatrice Hunter Cancer Research Institute, among others.

Jacqueline holds a PhD in Medical Sociology, a Master of Arts in Sociology and Bachelor of Arts degrees in Sociology and Anthropology. They have served as the Head of the Health Promotion Division and Interim Director of Dalhousie's School of Health and Human Performance, as Co-Director of the Atlantic Interdisciplinary Research Network in the Social and Behavioral Aspects of HIV and HCV, as a Founding Fellow of the MacEachen Institute for Public Policy and Governance, and Director of Dalhousie's Gender and Health Promotion Studies (GAHPS) Unit, which conducts multisectoral health promotion research and health policy analyses in relation to gender and sex as key determinants of health.

Dr. Emily Black

Dr. Emily Black received a Bachelor of Science in Pharmacy from Dalhousie University in 2007, an accredited Canadian Pharmacy Residency through Capital Health and Dalhousie University in 2008, and a post-graduate PharmD from the University of British Columbia in 2011. Currently, Emily is an Associate Professor with the College of Pharmacy at Dalhousie University. Emily also has affiliated scientific appointments with NS Health, IWK Health, and the Maritime SPOR Support Unit. Emily has an active program of research that focuses on antimicrobial utilization and stewardship. Emily also has a clinical cross appointment with IWK Health where she provides clinical pharmacy services in the emergency department and most recently with the COVID-19 vaccine clinic.

Oral Presentations

Time of presentation	Presenter	Title of Abstract
9:30-9:45	Melissa Andrew	FRAILTY, AGE AND OUTCOMES DURING WAVES 1-3 OF THE COVID-19 PANDEMIC; REPORT FROM THE CIRN SERIOUS OUTCOMES SURVEILLANCE (SOS) NETWORK
9:45-10:00	Anima Mayavannan	INVESTIGATING THE FUNCTIONAL ROLE OF TOLL-LIKE RECEPTOR 2 IN CHLAMYDIA PATHOGENESIS
10:00-10:15	Alexa Davis	UNDERSTANDING THE EFFECTS OF COVID-19 PUBLIC HEALTH OUTBREAK CONTROL POLICY IMPLEMENTATION ON NOT-FOR-PROFIT ORGANIZATIONS, PUBLIC HEALTH PRACTITIONERS AND THE SERVICES THEY PROVIDE TO HOMELESS POPULATIONS IN NOVA SCOTIA
10:15-10:30	Daniel Median-Luna	MOBILIZATION OF MEMORY NATURAL KILLER CELLS IN CANCER IMMUNOTHERAPY
10:30-10:45	Stephana Moss	FACTORS AFFECTING COVID-19 VACCINE HESITANCY AMONG HEALTHCARE PROVIDERS IN 23 COUNTRIES
10:45-11:00	BREAK	
11:00-11:15	Sarah Kim	ANTIMICROBIAL APPROPRIATENESS FOR PATIENTS WITH COVID-19: A RETROSPECTIVE OBSERVATIONAL STUDY
11:15-11:30	Beth MacDonald	USE OF SKIN TESTING IN EVALUATION OF PATIENTS WITH ADVERSE EVENTS FOLLOWING IMMUNIZATION: A CANADIAN IMMUNIZATION RESEARCH NETWORK STUDY
11:30-11:45	Henrique Pott-Junior	THE IMPACT OF COVID-19 VACCINATION ON CASE FATALITY RATES IN A CITY IN SOUTHERN BRAZIL
11:45-12:00	Alexa Wilson	KSHV E3 UBIQUITIN LIGASE K3 DOWNREGULATES THE CELLULAR STRESS SENSOR PERK.
12:00-12:15	Tiffany Fitzpatrick	ASSESSMENT OF PATIENTS WITH ADVERSE EVENTS FOLLOWING COVID-19 VACCINATION: PRELIMINARY DATA FROM THE SPECIAL IMMUNIZATION CLINIC (SIC) NETWORK

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

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Oral Presentation Abstracts

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

Oral Presentation 1

Title: FRAILTY, AGE AND OUTCOMES DURING WAVES 1-3 OF THE COVID-19 PANDEMIC; REPORT FROM THE CIRN SERIOUS OUTCOMES SURVEILLANCE (SOS) NETWORK

Authors: Andrew MK, LeBlanc JJ, Wilson K, McGeer A, McElhaney JE, Hatchette TF, ElSherif M, MacKinnon-Cameron D, Godin J, Ambrose A, Boivin G, Valiquette L, Trottier S, Loeb M, Smith S, Katz K, McCarthy A, McNeil SA

Affiliation: Department of Medicine (ID and Geriatrics), CCfV

Introduction: Frailty is a holistic measure of health status which influences risk, disease expression, and outcomes of illnesses including COVID-19. Here we report characteristics, including frailty, and outcomes of adults admitted to Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS) Network hospitals with COVID-19 during pandemic waves 1-3.

Methods: Patients with laboratory-confirmed COVID-19 admitted to eleven sites in Ontario, Quebec, Alberta and Nova Scotia up to August 31, 2021 were enrolled in this prospective observational cohort study. Waves varied slightly by jurisdiction, but were defined as W1:March 1-August 31,2020, W2:September 1,2020-Feb 28,2021 and W3:March 1,2021-August 31,2021. Key measures included age, Clinical Frailty Scale (1-3=fit, 4=vulnerable, 5=mildly frail, 6=moderately frail, 7=severely frail), demographics, and vaccination status. Outcomes of interest included intensive care unit admission and survival.

Results: Among 5508 patients, mean age in W1 was 68.8 (95%CI:67.5-70.1) vs. 71.3(70.6-71.9) in W2 and 60.7(59.9-61.5) in W3. The full spectrum of frailty was represented in both younger and older age groups. Frailty was highest in W2, with mean CFS 4.5(4.4-4.5), and decreased in W3, with CFS 3.8(3.7-3.9). Mortality was higher in W1(20.8%) and W2(22.8%) compared with W3(10.6%). Patients who died were older and frailer than the mean in each wave, though in W3 the mean CFS of those who died (4.8) was < mildly frail.

Conclusions: Frailty of patients admitted with COVID-19 to Canadian hospitals decreased in the third wave. This is likely due to multiple factors including vaccination program targeting (in the earliest phases of programmatic roll-out), higher vaccine uptake in older age groups and among those with multiple medical conditions, and emergence of Variants of Concern which resulted in more severe illness in younger, less frail, individuals in later waves. Frailty is a critical clinical factor in predicting outcomes of COVID-19, which should be considered in research and clinical settings.

Oral Presentation 2

Title: INVESTIGATING THE FUNCTIONAL ROLE OF TOLL-LIKE RECEPTOR 2 IN *CHLAMYDIA* PATHOGENESIS

Authors: Mayavannan A[1,2], Marshall JS[1], Wang J[1,2].

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

Introduction: *Chlamydia trachomatis* (*Ct*) is the most common STI and causes serious complications in women such as chronic pelvic pain, Pelvic Inflammatory Disease (PID), ectopic pregnancy and infertility. Toll-Like Receptor 2 (TLR2) is a pattern recognition receptor expressed widely on immune cells and structural cells. TLR2 binds to *Ct* and activates innate and adaptive host immune responses. Certain TLR2 haplotypes and polymorphisms have been shown to confer risk to *Ct*–associated infertility in women. The reported roles of TLR2 in protecting from reproductive tract tissue damage has been conflicting and its functional role in host responses to *Ct* infection remains an unresolved question. We hypothesized that the absence of a functional TLR2 protein could lead to dysregulated protective immune responses and consequentially result in long-term and irreversible tissue damage.

Methods: To characterize the functional role of TLR2, mice with or without the expression of TLR2, (WT and TLR2KO respectively), were infected with *Chlamydia muridarum* (*Cm*), a mouse adapted strain of *Ct* and innate and adaptive immune responses were examined by different immunological assays.

Results: Cysts formed in the oviduct of mice; a characteristic representation of cysts formed in the fallopian tubes of humans were comparable between the strains early on and interestingly the absence of TLR2 resulted in the formation of significantly larger cysts at 70-72 days post infection, indicating an essential role for the protein to protect from long term tubal blockage. While the TLR2KOs had comparable levels bacterial shedding in the lower uterine tract, they demonstrated dysregulated local immune responses with attenuated IL-6 response, increased Type 1 and Type 2 responses and longer-term inflammation compared to the WT controls. Additionally, TLR2KOs had dampened type 1 and type 2 systemic responses and were especially incapable of producing type 17 response. Type 17 response was recovered when mice were reconstituted with TLR2+/+ bone marrow derived myeloid cells.

Significance: These results together show a critical role for TLR2 in steering protective local and systemic immune responses. Moving forward, we will be doing immune profiling by immunohistochemistry on samples collected at various time points, to better understand the functional role of TLR2 in regulating innate and adaptive immune responses and resolution of cysts.

Oral Presentation 3

Title: UNDERSTANDING THE EFFECTS OF COVID-19 PUBLIC HEALTH OUTBREAK CONTROL POLICY IMPLEMENTATION ON NOT-FOR-PROFIT ORGANIZATIONS, PUBLIC HEALTH PRACTITIONERS, AND THE SERVICES THEY PROVIDE TO HOMELESS POPULATIONS IN NOVA SCOTIA

Authors: Davis A, Halperin D, Condran B, Kervin M, Salter K, Di Castri A, Halperin SA

Affiliation: Canadian Center for Vaccinology

Introduction: When the coronavirus disease of 2019 (COVID-19) was declared a pandemic, public health outbreak control policies were instrumental in containing and controlling the rapid spread of disease. However, the policies designed to mitigate the impact of the virus have adversely affected people experiencing homelessness.

Methods: In this qualitative case study, we sought to understand how service providers in the non-profit sector interpret, conceptualize, and implement COVID-19 public health policies. We used a nested approach to describe the nuances in rural and urban areas of Nova Scotia. We collected 11 documents (policy documents, communication materials, etc.), did 11 semi-structured interviews with public health practitioners, and staff and leadership of not-for-profit organizations, and analyzed resulting data using thematic analysis.

Results: Study findings capture the intersecting and complex needs of people experiencing homelessness during the pandemic. Living in a congregate and transient setting with limited access to personal protective equipment, handwashing, and technology posed barriers to implementing and adhering to policies. Innovative strategies were therefore necessary to support people experiencing homelessness. The altered working conditions and responsibilities also led to personal impacts on service providers. Participants emphasized the need to increase sustainable funding and resources and elicit input from front-line service providers to create and implement equitable and feasible public health policies.

Conclusion: The results of this project may inform context-specific pandemic preparedness and response plans during COVID-19 and future public health emergencies. Ultimately, to protect people experiencing homelessness during periods of upheaval and crisis, we need to focus on housing across Nova Scotia and keeping people housed through supportive policies.

Oral Presentation 4

Title: MOBILIZATION OF MEMORY NATURAL KILLER CELLS IN CANCER IMMUNOTHERAPY

Authors: Medina-Luna D, Gamage G, Scur M, Zein HS, Parsons BD, Makrigiannis AP

Affiliation: Department of Microbiology and Immunology, Dalhousie University, 5850 College Street, Halifax Nova Scotia, Canada.

Introduction: Immunological memory has long been exclusively attributed to T and B lymphocytes; however, we now know that natural killer (NK) cells also possess an analogous function. Studies of Rag-1-deficient mice (*Rag1*$^{-/-}$), which lack T and B cells, provided evidence of NK cell-mediated immunological memory. As NK cells also possess a natural capacity to eliminate tumour cells, we set out to define the role of NK cell memory in anti-cancer immune responses using NK cell-targeted cancer immunotherapy through immunization.

Methods: *Rag1*$^{-/-}$ mice (n=15) were immunized with the $E7_{49-57}$ RAHNIVYTIF (R9F) peptide from Human Papillomavirus 16, using the proprietary DepoVax (DPX) vaccine formulation, (IMV, Inc., NS Canada). Age-matched *Rag1*$^{-/-}$ mice (n=15) treated with the DPX vehicle alone served as controls. Sixteen days after immunization, all mice were flank-injected with C3 tumour cells, which express the R9F antigen. Tumour appearance and tumour growth rates were recorded. To determine the antigen specificity of NK cell memory, *Rag1*$^{-/-}$ mice (n=15) were immunized with the chicken-ovalbumin model antigen $OVA_{257-265}$ SIINFEKL (DPX-SIINFEKL) or DPX vehicle (n=15). Mice for these experiments were implanted with C3 cells that express the ovalbumin gene and present the SIINFEKL antigen (C3-OVA cells). For all groups, tumour appearance and tumour growth rates were recorded.

Results: *Rag1*$^{-/-}$ mice vaccinated with DPX-R9F had better protection against C3 tumour development, with 60% remaining tumour-free, in comparison to the DPX vehicle control cohort, in which all mice developed tumours. Additionally, the tumour growth rate in DPX-R9F immunized mice was significantly slower than in the control cohort. Furthermore, we found 60% of mice immunized with DPX-SIINFEKL and challenged with C3-OVA remained tumour-free, indicating that tumour protection could be induced by distinct antigens.

Conclusions: Our preliminary results suggest that DPX-R9F or DPX-SIINFEKL immunization induces antigen-specific protection against tumour development in mice in a T cell- and B cell-independent manner. By demonstrating that memory NK cells have a role in protection against tumour development, future cancer immunotherapies could be improved by priming not only T cells but also NK cells, creating in this way a new therapeutic approach.

Oral Presentation 5

Title: FACTORS AFFECTING COVID-19 VACCINE HESITANCY AMONG HEALTHCARE PROVIDERS IN 23 COUNTRIES

Authors: Moss SJ, Parsons Leigh J, White TM, Picchio CA, Rabin KH, Ratzan SC, Wyka K, El-Mohandes A, Lazarus JV

Affiliation: Applied Health Research & Knowledge Mobilization Lab, FACULTY OF HEALTH, Dalhousie University, Halifax, NS

Introduction: Several early COVID-19 studies aimed to assess the potential acceptance of a vaccine among healthcare providers, but relatively few studies of this population have been published since the vaccines became widely available. Vaccine safety, speed of development, and low perceived disease risk were commonly cited as factors for COVID-19 vaccine hesitancy among this group.

Methods: In a secondary analysis based on a cross-sectional, structured survey, authors aimed to assess the associations between self-reported vaccine hesitancy and a number of sociodemographic and COVID-19 vaccine perception factors using data from 3,295 healthcare providers (physicians, nurses, community health workers, other healthcare providers) in 23 countries.

Results: 494 (15.0%) of the participants reported vaccine hesitancy, of whom 132 (4.0%) would outright refuse to accept a COVID-19 vaccine. Physicians were the least hesitant. Vaccine hesitancy was more likely to occur among those with less than the median income and, to a lesser degree, younger age. Safety and risk concerns and lack of trust that vaccines would be equitably distributed were strongly associated with hesitancy, less so were concerns about the efficacy of COVID-19 vaccines.

Conclusions: Findings suggest a need to address safety and risk concerns through tailored messaging, training, and/or incentive approaches among healthcare providers, as well as the need for international and national vaccination efforts to ensure equitable distribution.

Oral Presentation 6

Title: ANTIMICROBIAL APPROPRIATENESS FOR PATIENTS WITH COVID-19: A RETROSPECTIVE OBSERVATIONAL STUDY

Authors: Kim S, Reid EK, MacAdam E, Murphy V, Bonnar P, Barrett L, Ramsey TD

Affiliation: Dalhousie University, Nova Scotia Health

Introduction: Antimicrobial use in patients infected with COVID-19 is not well-defined. Many factors, including the use of immunomodulatory therapies, may impact co-infection and secondary infection risk and antimicrobial prescribing. This study aimed to characterize antimicrobial appropriateness for patients admitted with or for COVID-19.

Methods: This single-centre retrospective chart review between April 1, 2021 and June 30, 2021, included adults admitted to the Queen Elizabeth II Health Sciences Centre during Nova Scotia's delta variant wave who received a systemic, non-SARS-CoV-2-directed antimicrobial after COVID-19 diagnosis. Patient charts were reviewed for demographics, infection, microbiological, COVID-19 therapy, and antimicrobial information. National Antimicrobial Prescribing Survey definitions were modified to assess antimicrobial appropriateness.

Results: One hundred and eighty-nine patients were identified in our chart review admitted with or for COVID-19. One hundred and nineteen, 63% (119/189), received a non-SARS-CoV-2-directed antimicrobial. Of the 116 patients eligible for assessment, 22% (25/116) required intensive care and 91% (106/116) were treated with COVID-19 immunomodulatory therapy: 91% (106/116) received corticosteroids and 34% (39/116) received both corticosteroids and tocilizumab. The most common antimicrobial indications were community acquired pneumonia (41/198), hospital acquired pneumonia (32/198), empiric influenza treatment (26/198), and bacteremia (19/198). Of the 276 antimicrobials prescribed, 256 (93%) were determined to be appropriate based on chart review: 184 were categorized as compliant with guidelines, 53 had a confirmed culture, and 19 were appropriate prophylaxis.

All patients had an infectious diseases (ID) consult and 43% (119/276) of antimicrobials were prescribed by an ID physician. Ceftriaxone (55/276), piperacillin/tazobactam (48/276), and intravenous vancomycin (33/276) were prescribed the most.

Conclusions: Nearly two-thirds of patients admitted with COVID-19 received a non-SARS-CoV-2-directed antimicrobial and over 90% were treated with immunomodulatory therapy. The majority of antimicrobials prescribed for inpatients with COVID-19 were deemed appropriate based on chart review.

Oral Presentation 7

Title: USE OF SKIN TESTING IN EVALUATION OF PATIENTS WITH ADVERSE EVENTS FOLLOWING IMMUNIZATION: A CANADIAN IMMUNIZATION RESEARCH NETWORK STUDY

Authors: MacDonald B[1,2], Muñoz C[3a], Sadarangani M[4,5], Cowan J[6], Zafack J[7], Upton J[8], Abdurrahman Z[9], McHenry M[10], Hildebrand K[5], Top KA[1,3,10] for the Special Immunization Clinic Network Investigators

Affiliation: [1]Canadian Center for Vaccinology, IWK Health Centre, Nova Scotia Health, Dalhousie University, Halifax, Nova Scotia, Canada [2]Faculty of Medicine, Dalhousie University [3]Department of Community Health and Epidemiology, Dalhousie University, Halifax, Nova Scotia, Canada [a]Current affiliation: Cardio-Respiratory Research Lab, McMaster University 1200 Main St W. Hamilton, Ontario, Canada [4]Vaccine Evaluation Center, BC Children's Hospital, University of British Columbia, Vancouver, British Columbia, Canada [5]Department of Pediatrics, Faculty of Medicine, University of British Columbia, Vancouver, 29 British Columbia, Canada [6]The Ottawa Hospital Research Institute, University of Ottawa, Ottawa, Ontario, Canada [7]Public Health Agency of Canada, Ontario, Canada [8]Division of Infectious Diseases, Hospital for Sick Children & Department of Pediatrics, 33 Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada [9]Department of Pediatrics, McMaster University, Hamilton, Ontario, Canada [10]Department of Pediatrics, Dalhousie University

Introduction: Vaccines may cause rare allergic reactions. The Special Immunization Clinic (SIC) Network evaluates patients with adverse events following immunization (AEFIs). Allergy skin testing is recommended for patients with an allergic-like event (ALE) within 4 hours or any AEFI within 1 hour of vaccination. We sought to determine frequency of positive skin tests, revaccination recommendations, and AEFI recurrences among participants assessed in the SIC Network (2013-2019).

Design and Methods: We analyzed SIC Network patients who required further doses of associated vaccine(s), underwent skin testing to a vaccine or excipient and consented to participate. Revaccinated participants were followed up for AEFI recurrence. Data on referral indication, medical history, vaccinations, AEFI details, skin test results and recurrences were collected. Skin test results were compared by skin test indication. Data were extracted from the SIC Network database for descriptive analysis.

Results: Analysis included 147 participants; 98 (67%) met skin test criteria. Among 49 participants tested outside of criteria, there were 22 ALE with onset ≥4h, 11 injection site reactions, 6 non-urticarial rash and 10 systemic AEFIs. Positive skin tests occurred in 25/98 (26%) participants who met criteria versus 11/49 (22%) who did not. Among participants with positive testing, revaccination was recommended to 15/25 (60%) who met criteria versus 7/11 (64%) who did not. Of those revaccinated, recurrences occurred in 5/13 (38%) versus 0/4 (p=0.261). Among participants with negative testing, 94% were recommended for revaccination and of those revaccinated, recurrences occurred in 0/53 who met criteria versus 3/22 (14%) who did not (p=0.023). No recurrences were serious.

Conclusions: Participants underwent skin testing for a range of AEFIs and most were recommended for revaccination irrespective of results. Having an indication for skin testing was associated with decreased AEFI recurrence risk among participants with negative skin tests.

Oral Presentation 8

Title: THE IMPACT OF COVID-19 VACCINATION ON CASE FATALITY RATES IN A CITY IN SOUTHERN BRAZIL

Authors: Pott-Junior H[1], Passarelli-Araujo H[2], Susuki AM[2], Olak AS[2], Pescim RR[2], Tomimatsu MFAI[3], Volce CJ [3], Neves MAZ[3], Silva FF[3], Narciso SG[3], Aschner M[4], Paoliello MMB[4], Urbano MR[2]

Affiliation: [1]Department of Medicine, Federal University of São Carlos (UFSCar), São Carlos, Brazil. [2] State University of Londrina (UEL), Londrina, PR, Brazil. [3] Municipal Health Department of Londrina, Parana, Brazil.; [4] Department of Molecular Pharmacology, Albert Einstein College of Medicine, Bronx, New York, USA.

Introduction: Recent studies have established that vaccination plays a significant role in reducing COVID-19-related deaths. Here, we investigated differences in COVID-19 case fatality rates (CFRs) among vaccinated and unvaccinated populations and analyzed whether the age composition of confirmed cases has a significant effect on the variations in the observed CFRs across these groups.

Methods: The study considered 59,853 confirmed cases and 1,687 deaths from COVID-19, reported between January 1st to October 20th, 2021, by the Health Department of Londrina, a city in Southern Brazil. We used Negative Binomial regression models to estimate CFRs according to vaccination status and age range.

Results: There are significant differences between the CFR for fully vaccinated and unvaccinated populations (IRR=0.596, 95% CI [0.460 - 0.772], $p<0.001$). Vaccinated populations experience fatality rates 40.4% lower than non-vaccinated. In addition, the age composition of confirmed cases explains more than two-thirds of the variation in the CFR between these two groups.

Conclusions: Our novel findings reinforce the importance of vaccination as an essential public health measure for reducing COVID-19 fatality rates in all age groups. The results also provide means for accurately assessing differences in CFRs across vaccinated and unvaccinated populations. Such assessment is essential to inform and determine appropriate containment and mitigation interventions in Brazil and elsewhere.

Oral Presentation 9

Title: KSHV E3 UBIQUITIN LIGASE K3 DOWNREGULATES THE CELLULAR STRESS SENSOR PERK

Authors: Wilson A, McCormick C

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

Introduction: Kaposi's sarcoma-associated herpesvirus (KSHV) causes multiple human cancers and is one of seven known human oncoviruses. Its dormant (latent) and productive (lytic) life cycles are both important for oncogenesis and KSHV virus-host interactions remain incompletely understood. We observed that KSHV dysregulates the cellular unfolded protein response (UPR), which regulates cell stress. The UPR is coordinated by three sensors, PERK, IRE1 and ATF6, which survey and respond to changes in protein synthesis in the endoplasmic reticulum. During lytic replication the UPR is initially activated, but then promptly turned off. It is unclear how the virus turns off the UPR and how this benefits the virus. Notably, we observe a drop in steady-state PERK protein levels during viral infection, suggesting the virus has evolved a mechanism to target the PERK protein. Using single gene expression studies, we aim to understand the KSHV-dependent mechanisms behind PERK downregulation and reveal how this viral countermeasure enhances viral fitness.

Methods: 293T cells were transduced with lentiviruses encoding KSHV genes and PERK protein levels were assessed by immunoblotting. Flow cytometry and immunofluorescence assays were used to confirm that K3 expression was sufficient to downregulate PERK protein levels. Drugs were used to investigate the loss of PERK including MG132, 26S-proteasome inhibitor, and hydroxychloroquine (Hcq), lysosomal acidification inhibitor. Site-directed mutagenesis of K3 and PERK-FLAG constructs were created to probe the K3-PERK interaction.

Results: By testing individual KSHV proteins for their ability to regulate the UPR, we found that the viral K3 protein could inhibit the UPR by targeting the UPR sensor, PERK. K3 is a RING-CH ubiquitin E3 ligase unique to KSHV that promotes the polyubiquitination of host immune synapse molecules required for anti-viral responses. These polyubiquitinated proteins are then trafficked to the lysosome and degraded. Notably, KSHV also encodes a homologue of K3, denoted K5. K5 has a similar role in sending immune synapse molecules for degradation in the lysosome. Our data suggests that K3 is sufficient to downregulate PERK, yet K5 does not have the same effect, suggesting a novel role of K3. My preliminary studies show that Hcq, an inhibitor of lysosomal acidification, rescues PERK protein levels in the presence of K3.

Conclusions: We uncovered a novel function of K3 during KSHV infection. Presently, we continue to probe this mechanism to determine if PERK is targeted to lysosomes for degradation like other K3 targets. Our experiments highlight a novel means of viral control over infected cells and could have impacts on both KSHV oncogenesis and disease progression in infected individuals.

Oral Presentation 10

Title: ASSESSMENT OF PATIENTS WITH ADVERSE EVENTS FOLLOWING COVID-19 VACCINATION: PRELIMINARY DATA FROM THE SPECIAL IMMUNIZATION CLINIC (SIC) NETWORK

Authors: Fitzpatrick T, Top KA, on behalf of the Special Immunization Clinic (SIC) Network Investigators

Affiliation: Canadian Center for Vaccinology, IWK Health Centre, Nova Scotia Health Authority, and Dalhousie University, Halifax, NS

Introduction: Experiencing an adverse event following immunization (AEFI) can increase vaccine hesitancy among patients and health professionals concerned about a more severe recurrent event following revaccination. Infectious disease physicians and allergists in the Canadian Special Immunization Clinic (SIC) Network developed standard protocols for evaluation and revaccination of patients with prior AEFIs. We analyzed preliminary data for patients aged 12+ evaluated for AEFIs following COVID-19 vaccination as of October 2021.

Methods: Patients referred to one of 10 SICs for an AEFI of special interest following COVID-19 vaccination were eligible for inclusion: suspected hypersensitivity reactions; acute onset neurologic or cardiac events; acute onset coagulation disorders; acute onset organ dysfunction; and other severe local or systemic symptoms. Following individual consent, data were transferred to a central database.

Results: Of 250 enrolled patients, 83% were referred following their first vaccine dose. Most patients (72%) were referred following BNT162b2 vaccination (n=179); 49 (20%) and 22 (9%), respectively, following mRNA-1273 and ChAdOx1. Reasons for referral varied by product. Among BNT162b2 and mRNA-1273 referrals, hypersensitivity (45% and 35%, respectively) and cardiac events (18% and 24%) were most common; hematologic disorders (41%) and neurologic events (36%) were most common among ChAdOx1 referrals. Only 6% of assessed AEFIs were deemed serious (based on PHAC classification); most had moderate (50%) or low (20%) impact on daily activities. Revaccination was recommended for 66% of patients, including 77% of hypersensitivity and 32% cardiac referrals.

Conclusions: Patients with AEFIs benefit from clinical assessment by physicians with vaccine expertise. AEFIs referred to the SIC Network were primarily low-moderate impact and COVID-19 revaccination was widely recommended. Follow up of revaccination uptake and AEFI recurrence is ongoing.

Poster Abstracts

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

Poster 1

Title: SARS-COV-2 MEMBRANE AND ENVELOPE PROTEINS INHIBIT SPIKE-MEDIATED ACTIVATION OF ATF6

Authors: Caddell T, Pringle ES[1,*], McCormick C[1]

Affiliation: [1]Department of Microbiology & Immunology, Dalhousie University.*Equal Contribution

Introduction: The ER-Golgi intermediate compartment (ERGIC) mediates anterograde and retrograde trafficking between the ER and Golgi. It is also a central hub for signaling processes that transit through the secretory pathway, influencing stress signaling, cholesterol regulation, interferon production, and inflammasome assembly. We hypothesize human coronavirus (hCoV) assembly at the ERGIC threatens the proper function of these pathways.

Methods: SARS-CoV-2 structural proteins were overexpressed to determine activation or inhibition of ATF6 using a luciferase reporter plasmid. Furthermore, cells were infected with hCoV-OC43, and cell lysates collected to detect the presence of full-length ATF6 or the activated cleaved form ATF6-N via immunoblotting to measure ATF6 activation during infection. Finally, cells were infected with hCoV-OC43 or hCoV-229E and treated with the drug AA147. At 24 hours post infection supernatants were collected and used to measure viral replication via $TCID_{50}$.

Results: We discovered hCoV structural proteins affect the function of the stress responsive ATF6 pathway. ATF6 detects ER stress and traverses the ERGIC to be processed at the Golgi, generating the ATF6-N transcription factor that transactivates unfolded protein response (UPR) genes. We found the SARS-CoV-2 Spike protein selectively activates ATF6, but membrane (M) and envelope (E) proteins inhibit this activation. Furthermore, we observed ATF6 is not activated during hCoV-OC43 infection. Chemical activation of ATF6, using the drug AA147, reduced replication of hCoV-OC43 and hCoV-229E, suggesting ATF6 activation elicits an antiviral gene expression program.

Conclusions: By studying interactions between hCoV structural proteins and host signaling proteins at the ERGIC, we hope to understand how hCoV replication impacts host cell physiology and responses to infection. Current SARS-CoV-2 vaccines direct Spike expression in the absence of other structural proteins like E and M. Based on our findings, we expect that vaccine-mediated Spike expression may activate ATF6, which might be important for generating robust antiviral immune responses. As next generation vaccines incorporate other CoV structural proteins, it will be important to determine how they affect Spike antigenicity, which may be influenced by host signaling pathways that traverse the ERGIC.

Poster 2

Title: SAFETY MONITORING OF COVID-19 VACCINES IN THE PEDIATRIC POPULATION: ESTIMATING THE ASSOCIATION BETWEEN COVID-19 VACCINATION AND FEBRILE SEIZURE VIA THE CANADIAN IMMUNIZATION MONITORING PROGRAM–ACTIVE (IMPACT)

Authors: Hassan F, Top KA, for the Canadian Immunization Monitoring Program Active Investigators

Affiliation: Canadian Center for Vaccinology and Department of Community Health & Epidemiology, Dalhousie University

Introduction: Phase III trials of COVID-19 vaccines for children under 5 years of age are ongoing with results expected this spring. To ensure public confidence in pediatric vaccination program, early detection, analysis, and communication of adverse events following immunization (AEFIs) is utterly important. Febrile seizure is an AEFI of interest as it is common in young children and has been rarely associated with certain vaccines.

Methods: We are conducting prospective active surveillance for febrile seizure for children aged <7 years who visited emergency department (ED) and/or were hospitalized at an IMPACT center(s)- a network of 13 pediatric tertiary care centers in Canada. At each center, trained nurses screen ED visit/hospitalization records for cases of fever (temperature ≥38.0°C) and physician diagnosed febrile seizure. Immunization records are retrieved from the medical record/public health. The self-controlled case series (SCCS) method will be used to estimate the relative incidence of febrile seizure in the risk window (0-3 days) when an adverse reaction to the vaccine is biologically plausible versus the remote "control window" (>7 days pre- or post-vaccination) when the vaccine cannot be plausibly implicated. Comparisons are made within individuals; thus, subjects act as their own control, implicitly adjusting for time independent confounding. Conditional Poisson regression models will be adjusted for age and season. In descriptive analysis, ED visits and hospitalizations for febrile seizure will be reported by age, sex, province, and clinical features (e.g., comparison by ED visit versus hospitalization, symptoms, COVID-19 vaccine given alone versus with other vaccines).

Results: The study will contribute to understanding the safety profile of COVID-19 vaccines in the pediatric population to facilitate informed public health decision-making and support public confidence.

Conclusions:

Poster 3

Title: INVESTIGATING THE ROLES OF UNFOLDED PROTEIN RESPONSE TRANSCRIPTION FACTORS IN Influenza A VIRUS INFECTION

Authors: Butova A[1], McCormick C[1]

Affiliation: [1]Department of Microbiology & Immunology, Dalhousie University

Introduction: All enveloped viruses encode transmembrane proteins that are synthesized, folded and processed at the endoplasmic reticulum (ER). The capacity of the ER to support these activities is tightly regulated by the unfolded protein response (UPR). The UPR is governed by three ER-localized sensor proteins (ATF6, IRE1 and PERK) that sense the accumulation of unfolded proteins in the ER and initiate synthesis of transcription factors (ATF6-N, XBP1s and ATF4, respectively) that coordinate a gene expression program that increases ER capacity to restore proteostasis. Influenza A virus (IAV) encodes transmembrane glycoproteins that are folded and processed in the ER. Studies to date suggest a complex relationship between IAV and the UPR, whereby viral replication can be arrested by UPR-inducing drugs, but IRE1 activity is required to support efficient viral replication. Overall, interactions between IAV and the UPR remain poorly characterized. My goal is to advance understanding of how UPR pathway components affect IAV infection and to elucidate mechanisms of viral control of the UPR.

Methods: To investigate how different arms of UPR affect viral replication, A549 lung epithelial carcinoma cells were transduced with lentiviral constructs encoding ATF6-N, XBP1s or ATF4 and selected with puromycin. These cells were infected with IAV strain A/Puerto Rico/8/34(H1N1) at low MOI (0.01) or high MOI (3) and cell supernatants were collected at 6 hours post-infection (hpi), 12 hpi or 24 hpi and titered by plaque assay on MDCK cells using standard methods. RNA was harvested from cell lysates at each time point to measure the UPR and viral gene expression by RT-qPCR.

Results: We observed that expression of UPR transcription factors ATF6-N and XBP1s in A549 cells inhibited IAV replication and release of infectious virions compared to negative control A549 cells transduced with an empty lentiviral vector. Ongoing studies are focused on confirming these preliminary findings and investigating the stage of infection disrupted in cells expressing UPR transcription factors.

Conclusions: These studies will help us understand precisely which components of the UPR threaten viral replication and which viral processes are undermined. These studies will inform the next steps in identifying and characterizing potential antiviral components of the UPR and viral proteins that counter these antiviral responses.

Poster 4

Title: DEPENDENCY OF LY49 RECEPTORS IN NATURAL KILLER CELL MEMORY.

Authors: Gamage G, Medina-Luna D, Scur M, Zein HS, Parsons BD, Rahim MMA, Makrigiannis AP

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

Introduction: Immunological memory is a unique feature of the adaptive immune system. However, studies over the past decade revealed that natural killer (NK) cells, a subset of innate lymphoid cells, also mediate antigen-specific memory responses. Even though the existence of NK cell memory is established, the mechanism behind NK cell memory is yet to be discovered. Our lab previously found that the Ly49 receptors, a class-I MHC receptor family in mice, are critical for the formation of adaptive NK cell responses. To further elucidate the requirement for Ly49 receptors in NK cell memory, we investigated the contribution of individual Ly49 receptors and their defined MHC-I ligands in adaptive NK cell responses. Findings from this study will help us to better understand the mechanism behind the NK cell memory, thereby opening opportunities to exploit adaptive NK cell features in vaccine development and cancer immunotherapy.

Methods: We tested immunological memory responses to chemical haptens and peptides by contact hypersensitivity (CHS) ear swelling assays in mice. To test the role of Ly49 receptors in NK cell memory, we performed CHS ear swelling assays in mice that lack T and B lymphocytes (RagKO), and Ly49 receptors (RagKO Ly49KO). To study the contribution of specific Ly49s, we tested the role of Ly49C/I and Ly49G receptors. We performed CHS ear swelling assays in RagKO Ly49C/I mice to test the role of Ly49C/I and RagKO Ly49G KO H-2d mice to test the role of Ly49G in NK cell memory responses.

Results: We found that RagKO mice that lack the expression of all Ly49 receptors fail to generate recall responses to chemical haptens and peptides. However, mice that specifically lack Ly49G receptors showed no difference in ear swelling responses to haptens or peptides compared to controls. In contrast, ear swelling responses to haptens and peptides are completely lost in mice that specifically lack Ly49C/I receptors.

Conclusions: Overall, our findings show that the Ly49 receptor requirement for the formation of adaptive NK cell responses is not uniform. We observe that Ly49C/I receptors are critical for the generation of NK cell memory responses while Ly49G receptors, another highly expressed Ly49 receptor in mice, are dispensable for adaptive NK cell responses suggesting that NK cell memory may be intrinsic to select Ly49 receptors, such as Ly49C/I.

Poster 5

Title: IMPROVING ANTIMICROBIAL STEWARDSHIP IN THE TREATMENT OF *Streptococcus pneumoniae* RESPIRATORY INFECTIONS

Authors: Khan FM[1,2], O Allehebi Z[1,2], Shabi YM[1,2], Davidson RJ[1,2]

Affiliation: [1]Department of Pathology and Laboratory Medicine, Nova Scotia Health, Halifax, NS
[2]Faculty of Medicine, Department of Pathology, Dalhousie University, Halifax, NS

Introduction: In the clinical laboratory *S. pneumoniae* is frequently tested against oxacillin to predict susceptibility to penicillin. In isolates with an oxacillin zone < 20mm, penicillin is tested and if resistant, the assumption made by many clinicians is that amoxicillin will also be resistant. As such, oxacillin non-susceptible, penicillin resistant isolates may be managed with second-line agents such as macrolides or fluoroquinolones. These broader-spectrum agents potentially expose patients to more side effects and increases the risk of development of antimicrobial resistance. Oral amoxicillin could potentially be a narrower-spectrum option; however, susceptibilities are frequently not provided.

Methods: Susceptibility testing was performed on 64 oxacillin non-susceptible *S. pneumoniae* isolated from respiratory specimens by our clinical laboratory since 2010. Amoxicillin and penicillin diffusion gradient testing and susceptibility was interpreted using published clinical standards, Clinical Laboratory Standards Institute (CLSI).

Results: Of the 64 oxacillin non-susceptible isolates, 49% (N = 31) were penicillin resistant using oral penicillin MIC breakpoints. Testing against amoxicillin demonstrated that 97% (N = 62) were sensitive using the CLSI amoxicillin non-meningitis MIC breakpoints.

Conclusions: This study demonstrates that oral amoxicillin is often susceptible against oxacillin non-susceptible *S. pneumoniae* and that reporting only a penicillin result could potentially lead clinicians to prescribe broader spectrum agents when amoxicillin, a narrower therapeutic choice, might be a more favorable option. Clinical laboratories should consider testing both penicillin and amoxicillin against oxacillin non-susceptible *S. pneumoniae* in settings where an oral agent would be appropriate.

Poster 6

Title: A CASE OF CATALASE-POSITIVE *STREPTOCOCCUS*

Authors: Shabi YM, Khan FM, O Allehebi Z, Romeo T, MacKinnon B, Davidson R, Patriquin G

Affiliation: Department of Pathology and Laboratory Medicine, Nova Scotia Health and Dalhousie University. Halifax, Nova Scotia, Canada

Introduction: A 53-year-old man from Atlantic Canada with multiple comorbidities including T10-11 level paraplegia, bilateral below-knee amputations, and chronic renal failure, with a chronic left greater trochanteric ulcer, presented to the Emergency Department in the Fall of 2021 with fever, chills and night sweats (with labs shown in Table 1). He was discharged home on amoxicillin-clavulanic acid, pending blood culture results. Both sets of blood culture returned with chaining and clustering gram-positive cocci suggestive of Streptococci or Enterococci seen in smears from both aerobic and anaerobic vials and he was given ceftriaxone and metronidazole for possible mixed bacteremia.

Microbiology: Growth from a single set of blood culture bottles was identified as *Streptococcus mitis* and the other set grew tiny, whitish-grey, nonhemolytic colonies on sheep blood agar, chocolate agar and anaerobic sheep blood agar. The isolate was initially reported as *Streptococcus species* as MALD-TOF identified it as *Streptococcus equi,* 50/50%, ssp *zooepidemicus* and ssp *ruminatorum*. Agglutination testing revealed group B antigen. Catalase from broth culture and Mueller-Hinton agar was negative, but positive from both blood and chocolate agar. The isolate failed to identify on the BD Phoenix. The sensitivity revealed susceptibility to penicillin (MIC:0.032), ceftriaxone (MIC:0.125) and Vancomycin (MIC:0.5). Sequencing revealed the identification as *S. halichoeri.*

Case outcome: The patient completed 14 days of Ceftriaxone and Metronidazole. On follow-up assessment, his symptoms has resolved and wound has improved.

Conclusions: *S. halichoeri* is an unusual *Streptococcus* species as it can be catalase-positive. Frequently, it has been associated with canines and grey seals (*Halichoerus grypus*). Our patient has a pet dog and frequents Atlantic Ocean waters. Such isolates can be dismissed as Coagulase-negative Staphylococcus, especially from a non-sterile site. Thus, special attention should be applied when observing catalase-positive gram positive cocci that fail to identify as *Staphylococcus spp*.

Poster 7

Title: UNDERSTANDING *SHIGELLA FLEXNERI* INDUCED DENDRITIC CELL DEATH

Authors: Sherwood JT, Nelson A, Johnston B, Rohde J

Affiliation: Department of Microbiology and Immunology, Dalhousie University

Introduction: Bacteria of the genus *Shigella* cause a severe diarrheal disease known as shigellosis. Shigellosis kills hundreds of thousands each year, mostly children in the developing world. No vaccine exists against shigellosis and *Shigella*'s many serotypes, poor understanding of mechanisms of its immune evasion, and the lack of a good animal model have hindered vaccine development. *S. flexneri* uses a type III secretion system (T3SS) with ~30 effector proteins that manipulate host defense, entry, and immune evasion. Effector protein functions have been primarily investigated in epithelial cells but *S. flexneri* also infects immune cells including macrophages and dendritic cells (DCs). *S. flexneri* has been reported to promote the rapid death of DCs but the mechanisms by which this occurs, and the bacterial effectors responsible, are unknown. Here, we describe the role of two effectors in promoting DC death.

Methods: Murine derived dendritic cells were infected with *S. flexneri* strains at a multiplicity of infection of 10, incubated 1 hour, treated with gentamicin, then incubated 3 hours. DC death was measured via flow cytometry. DC death induced by individual effector mutants and double effector mutants were compared to wild-type (WT), a strain lacking a T3SS, and uninfected control conditions.

Results: The 4-hour infection protocol showed differences between each control strain. Knockout of individual effector mutants showed no difference to the WT. By contrast, mutants deleted for both effectors resembled the T3SS knockout phenotype.

Conclusions: Individual effectors alone do not contribute to *S. flexneri* induced DC death. However, their combined functions are important. The infection protocol described here allows for distinguishing differences in DC death for each control condition. Additionally, the double mutant experiment shows the efficacy of this method for investigating the redundancy of function among the repertoire of *S. flexneri* effectors.

Poster 8

Title: A CASE OF TRENCH FEVER- WITH NO TRENCH, AND NO FEVER

Authors: Grace N, LeBlanc JJ, McNeil S, Castonguay M, Patriquin G

Affiliation: Dalhousie University

Introduction: *Bartonella quintana (B. quintana)*, a gram-negative bacterium transmitted by human body louse, is the agent of trench fever during World War I and II. Several case reports have recently identified it as a cause of blood culture-negative endocarditis, particularly in patients with alcohol use disorder, homelessness, and poor hygiene.

Case: This is a case of an 80- year-old male laborer who developed severe aortic valve regurgitation resulting in heart failure from culture-negative endocarditis. Ten years prior, the patient also had a mitral valve repair due to severe mitral valve regurgitation. Pathological assessment of the aortic valve following its replacement showed changes consistent with native valve endocarditis, but no microorganisms were detected on tissue special stains. Therefore, the diagnosis of *B. quintana* was suspected and confirmed by 16S rRNA PCR and *Bartonella*-specific serology of the valve tissue. Following treatment with doxycycline and rifampin, patient recovered well and his *B. quintana* titers resolved.

Conclusions: *B.quintana* endocarditis is one of the causes of culture-negative endocarditis that is difficult to diagnose. The diagnosis requires a high level of clinical suspicion since specific serological and PCR tests are not routinely performed on excised valve tissue.

Poster 9

Title: INVESTIGATING THE HOST UFMYLATION PATHWAY IN INFLUENZA VIRUS INFECTION

Authors: Samaraweera EG[1], Caddell T[1] , McCormick C[1]

Affiliation: Dalhousie University, Department of Microbiology & Immunology[1] .

Introduction: Ubiquitin-Fold Modifier-1 (UFM1) is a Ubiquitin-like (UbL) protein that can be covalently linked to lysine residues on target proteins. The process of UFM1 conjugation (UFMylation) is mediated through an enzymatic cascade. While little is known about the consequences of protein UFMylation, the genes encoding the multicomponent UFMylation machinery are transactivated in response to endoplasmic reticulum (ER) stress, influencing proteostasis. Enveloped viruses, like influenza A viruses (IAVs), have complex interactions with ER proteostasis machinery. IAV encodes glycoproteins that can burden the protein folding machinery and trigger ER stress. Here, we demonstrate how UFMylation regulates IAV infection.

Methods: We used a CRISPR/Cas9 genome editing based approach to create human lung epithelial cell lines deficient in UFM1 or UFM1-specific cysteine protease 2 (UFSP2), which is required to deconjugate UFM1 from substrate proteins. These cell lines were infected with IAV to determine the effect of UFMylation on viral replication.

Results: Successful deletion of UFM1 and UFSP2 genes was demonstrated by the absence of the respective proteins in cell lysates. This also had the expected effect on the known UFMylation target ribosomal protein L26 (RPL26), whereby UFM1 deletion prevented RPL26 UFMylation and UFSP2 deletion caused the accumulation of high levels of UFMylated RPL26. UFSP2 deficiency had no effect on IAV replication and release of infectious progeny viruses. In contrast, UFM1 deficiency resulted in increased IAV replication at both high and low MOI infections.

Conclusions: The increase in IAV replication in the absence of UFM1 suggests an antiviral effect of UFM1. This supports information found in literature which shows that UFMylation is involved in promoting RIG-I signaling and induction of IFNs during RNA virus infections. These are integral components of the host innate immune response against IAV infections. Furthermore, UFSP2 is known to play a role in regulating resistance to IAV infection in mouse models. Contrastingly, my results suggest that UFSP2 may not play a role in IAV replication and release of infectious viruses in vitro. These findings reveal a molecular link between UFMylation and innate immune responses highlighting a potential pathway to be exploited for host-targeted antivirals.

Poster 10

Title: DEVELOPMENT OF A NEW HCOV-OC43 REVERSE GENETICS SYSTEM IN YEAST

Authors: Tooley T, Duguay BA, Sosa Diaz O, McCormick C

Affiliation: Dalhousie University

Introduction: Coronaviruses (CoVs) have large, positive-sense single-stranded RNA genomes that challenge conventional strategies for mutagenesis. The awesome power of yeast genetics has been adapted to the manipulation of large herpesvirus genomes and CoVs, including SARS-CoV-2. Here, we report progress in developing a transformation-associated recombination (TAR) mutagenesis system for the 'common cold' human CoV, HCoV-OC43.

Methods: Transformation-associated recombination (TAR), involves generating dsDNA copies of viral genome fragments with short stretches of homology at the ends that facilitate subsequent homologous recombination and assembly of complete genomes in *Saccharomyces cerevisiae*. We successfully generated three plasmids encompassing sequential, 7.2 kb portions of the *ORF1ab* gene (CoV1/2/3), a fourth plasmid with the *NS2* to *M* segment (CoV4), and a fifth plasmid containing the *N* gene (CoV6). We designed a set of plasmids for alternative "CoV5" fragments encoding EBFP2, mClover-H2B, mRuby-H2B, mCardinal, or Fluc reporter gene inserted into the intergenic region between the *M* and *N* genes.

Results: Herein, we show that we have successfully captured all HCoV-OC43 fragments and have completed partial assembly of fragments CoV4/5/6-mRuby-H2B into yeast artificial chromosomes. Work on partial assemblies for CoV1/2/3 and full genome assemblies using TAR is ongoing.

Conclusions: By creating a new reverse genetics system for mutagenesis and assembly of HCoV-OC43 genomes, we hope to increase the utility of this common surrogate for SARS-CoV-2 and share it widely with the research community to accelerate studies of host-virus interactions and aid development of antivirals and vaccines.

Poster 11

Title: THIOPURINES INHIBIT CORONAVIRUS SPIKE PROTEIN PROCESSING AND INCORPORATION INTO PROGENY VIRIONS

Authors: Duguay BA[1*], Pringle ES[1*], Ying S[1], Bui-Marinos MP[2], Mulloy RP[2], Landreth SL[3], Desireddy KS[1], Caddell T[1], Dolliver SM[1] , Slaine PD[1], Bearne SL[1], Falzarano D[3], Corcoran JA[2], Khaperskyy DA[1], McCormick C[1]

Affiliation: [1]Dalhousie University, [2]University of Calgary, [3]University of Saskatchewan/VIDO-InterVac, *Co-first authors.

Introduction: There is an outstanding need for broadly-acting antivirals to target emerging viruses. Host-targeted antivirals (HTAs) exploit viral dependence on host processes for efficient replication. In principle, HTAs have the potential for broad and sustained antiviral activity that is not so easily undermined by rapid viral evolution. We previously reported that 6-thioguanine (6-TG), a medication to treat acute leukemias and inflammatory bowel disease, inhibits influenza virus replication by activating host cell stress responses and inhibiting processing/accumulation of viral glycoproteins. Based on similar mechanisms of viral glycoprotein synthesis, we hypothesized that 6-TG may also limit human coronavirus (HCoV) replication.

Methods: Using many cell culture models, we examined the efficacy of 6-TG against multiple CoVs including: HCoV-OC43, HCoV-229E and SARS-CoV-2. We characterized the effects of 6-TG on productive viral replication, genomic RNA production (RT-qPCR), protein accumulation (western blotting and immunofluorescence), and virion morphology (transmission electron microscopy). 6-TG was also tested against ectopically expressed CoV Spike proteins to investigate changes in viral glycoprotein processing and accumulation and dependence on key host cell enzymes.

Results: 10 μM 6-TG treatment for 24-48 h caused a >10-fold inhibition in viral titres for all HCoVs tested, with a selectivity index of >72.7 against SARS-CoV-2. Similar decreases were also observed with viral genomic RNA and viral proteins (Nucleocapsid and Spike) following 6-TG treatment. Spike protein glycosylation was altered following 6-TG treatment, which could be corrected with treatment of cells with a pan-GTPase agonist, ML099; indicating that 6-TG acts through inhibition of one or more host GTPases. Finally, virus-like particles and virions released from cells displayed less Spike on their surfaces following 6-TG treatment, likely contributing to the observed decrease viral titre.

Conclusions: 6-TG is a potent alpha- and betacoronavirus antiviral. We document how 6-TG causes a prominent defect in CoV Spike protein glycosylation. Additional experiments using an inactive derivative, 6-TG-Me, and knockdown of HPRT1 showed that 6-TG needs to be metabolized to 6-TGTP exert these antiviral effects. The active form of 6-TG modulates GTPase activity to affect Spike glycosylation and virion incorporation, ultimately hindering virion assembly and infectivity. We believe 6-TG can be further improved as a promising HTA for multiple enveloped viruses. Our data highlight the GTPase-modulating effects of 6-TG and show that cellular GTPases are promising antiviral targets.

Poster 12

Title: EXPLORING THE IMPACT OF MEDIA AND INFORMATION ON SELF-REPORTED INTENTIONS TO VACCINATE AGAINST COVID-19: A QUALITATIVE INTERVIEW-BASED STUDY

Authors: FitzGerald EA, Moss SJ, Halperin D, Mizen SJ, Fiest KM, DiCastri A, Stelfox HT, Halperin SA, Leigh JP

Affiliation: Dalhousie University, Faculty of Health, Department of Health Administration

Introduction: The World Health Organization declared vaccine hesitancy a top threat to global health following resurgence of vaccine-preventable diseases (e.g., measles) close to eradication in many countries. Vaccines are effective in preventing severe illness, hospitalization, and death from COVID-19, yet there remains a small proportion of the eligible population who choose not to vaccinate. Social media and online news sources are opportunities for targeted public health interventions to improve vaccine uptake. This study reports the results of a semi-structured interview study that explored the influence of media and information on individuals' self-reported intentions to vaccinate against COVID-19.

Methods: A qualitative descriptive study was employed to gain insight from a diverse group of individuals. Adult participants were recruited through a related COVID-19 study; we used a maximum variation sampling technique and purposively sampled participants based on demographics. Interviews were conducted from February 2021 to May 2021. Themes from interviews were summarized with representative quotations according to the 3C Theoretical Framework (Confidence, Complacency, Convenience).

Results: Key themes identified following thematic analysis from 60 participants included: vaccine safety, choice of vaccine, fear mongering, trust in authority, and belief in vaccinations (Confidence); delaying vaccination (Complacency); and confusing information, and access to vaccines and information (Convenience). While most participants intended to vaccinate, many expressed concerns and hesitancy surround the COVID-19 vaccine.

Conclusions: COVID-19 vaccine hesitancy prevents universal immunization and contradictory messages in media are a source of concern and fear. The success of future vaccine campaigns will depend upon authorities' ability to disseminate accessible, detailed, and consistent information promoting public confidence.

Poster 13

Title: FRAILTY, AGE AND OUTCOMES DURING WAVES 1-3 OF THE COVID-19 PANDEMIC; REPORT FROM THE CIRN SERIOUS OUTCOMES SURVEILLANCE (SOS) NETWORK

Authors: Andrew MK, LeBlanc J, Wilson K, McGeer A, McElhaney JE, Hatchette TF, ElSherif M, MacKinnon-Cameron D, Godin J, Ambrose A, Boivin G, Valiquette L, Trottier S, Loeb M, Smith S, Katz K, McCarthy A, **McNeil SA**

Affiliation: Department of Medicine (ID and Geriatrics), CCfV

Introduction: Frailty is a holistic measure of health status which influences risk, disease expression, and outcomes of illnesses including COVID-19. Here we report characteristics, including frailty, and outcomes of adults admitted to Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS) Network hospitals with COVID-19 during pandemic waves 1-3.

Methods: Patients with laboratory-confirmed COVID-19 admitted to eleven sites in Ontario, Quebec, Alberta and Nova Scotia up to August 31, 2021 were enrolled in this prospective observational cohort study. Waves varied slightly by jurisdiction, but were defined as W1:March 1-August 31,2020, W2:September 1,2020-Feb 28,2021 and W3:March 1,2021-August 31,2021. Key measures included age, Clinical Frailty Scale (1-3=fit, 4=vulnerable, 5=mildly frail, 6=moderately frail, 7=severely frail), demographics, and vaccination status. Outcomes of interest included intensive care unit admission and survival.

Results: Among 5508 patients, mean age in W1 was 68.8 (95%CI:67.5-70.1) vs. 71.3(70.6-71.9) in W2 and 60.7(59.9-61.5) in W3. The full spectrum of frailty was represented in both younger and older age groups. Frailty was highest in W2, with mean CFS 4.5(4.4-4.5), and decreased in W3, with CFS 3.8(3.7-3.9). Mortality was higher in W1(20.8%) and W2(22.8%) compared with W3(10.6%). Patients who died were older and frailer than the mean in each wave, though in W3 the mean CFS of those who died (4.8) was < mildly frail.

Conclusions: Frailty of patients admitted with COVID-19 to Canadian hospitals decreased in the third wave. This is likely due to multiple factors including vaccination program targeting (in the earliest phases of programmatic roll-out), higher vaccine uptake in older age groups and among those with multiple medical conditions, and emergence of Variants of Concern which resulted in more severe illness in younger, less frail, individuals in later waves. Frailty is a critical clinical factor in predicting outcomes of COVID-19, which should be considered in research and clinical settings.

Poster 14

Title: CYTOKINE PROFILING OF ADULTS WITH COVID-19 FROM THE ILLNESS ONSET TO HOSPITAL ADMISSION

Authors: Pott-Junior H[1]; Luporini RL[1,2], de A. Rodolpho JM[3], Moreno Martin ACB[4], Cominetti MR[4], de Freitas Anibal F[2,3]

Affiliation: [1]Department of Medicine, [2]Biotechnology Graduate Program, [3]Department of Biological Sciences Parasitology, [4]Department of Gerontology, Federal University of São Carlos (UFSCar), São Carlos, Brazil.

Introduction: COVID-19 presents a broad spectrum of manifestations. However, it is unclear which factors are associated with disease progression towards severe conditions. To address this, we evaluated the relationship between different cytokines and inflammatory markers with disease severity, considering the time from the illness onset to hospital admission.

Methods: This is a single-center cross-sectional study at the Federal University of São Carlos from July to December 2020. Inclusion criteria were adult subjects with a positive RT-PCR test for SARS-CoV-2 infection and less than ten days from the illness onset to hospitalization. Data collection occurred within 12 hours of hospital admission and included: sociodemographic and clinical data and laboratory tests results. Disease severity assessment followed the recommendations set forth by the WHO's COVID-19 Clinical management living guidance. We also collected a sample of venous blood to analyze systemic markers of inflammation (IL-2, IL-4, IL-6, IL-10, IFN-γ, and TNF-α).

Results: This study included a total of 179 participants with a median age of 58 years old. Most were males (58.1%), with a median Charlson Comorbidity Index of 2 (range, 0 - 8), and about a fifth (19%) of them presented high comorbidity (index ≥ 5). Most of the participants were not hypertense (52.5%), diabetic (76.5%), had no cardiovascular diseases (84.4%), or chronic lung diseases (88.3%). We observed significant differences between severity groups in almost all parameters, except for IL-4 and TNF-α. Serum levels of LDH and IL-10 were significantly different between all groups (p adjusted < 0.05 in all pairwise comparisons). Lymphocyte count, albumin to globulin ratio, CRP, IL-2, and IFN-γ were significantly different in mild disease compared to the others, but there was no significant difference between moderate and severe disease. There was a significant difference in IL-6 between mild and severe groups but not between mild and moderate. D-dimer was also significantly different in the severe disease compared to the others.

Conclusions: IL-10 and LDH seem to play a relevant role in COVID-19, reflecting the continuous and dynamic interplay between viral infection and the immune response and its consequences. Furthermore, IL-2 emerges as a potential marker for mild cases.

Poster 15

Title: A PHASE 3, MULTICENTER, RANDOMIZED, DOUBLE-BLIND, ACTIVE-COMPARATOR-CONTROLLED STUDY TO EVALUATE THE SAFETY, TOLERABILITY, AND IMMUNOGENICITY OF A 4-DOSE REGIMEN OF V114 IN HEALTHY INFANTS (PNEU-PED)

Authors: Lupinacci R[1], Rupp R[2], Wittawatmongkol O[3], Jones J[4], Quiñones J[5], Ulukol B[6], Dagan R[7], Richmond P[8], Stek J[1], Romero L[1], Koseoglu S[1], Tamms G[1], McFetridge R[1], Li J[1], Cheon K[1], Musey L[1], Banniettis N[1], Bickham K[1] for the V114-029 (PNEU-PED) study group

Affiliation: [1]Merck & Co., Inc., Kenilworth, NJ, USA; [2]University of Texas Medical Branch, Galveston, TX, USA; [3]Mahidol University, Bangkok, Thailand; [4]Wasatch Pediatrics, Murray, UT, USA; [5]Clinical Research of Puerto Rico, Guayama, Puerto Rico; [6]Ankara University, Ankara, Turkey; [7]Ben-Gurion University, Beer-Sheva, Israel; [8]University of Western Australia, Perth, Australia

Introduction: Pneumococcal disease (PD) remains a major health concern globally. Pneumococcal conjugate vaccines (PCVs) confer protection against PD caused by most vaccine serotypes, but residual disease remains partly due to non-vaccine serotypes. V114 is a 15-valent PCV containing all 13 serotypes in Prevnar 13™ (PCV13) and serotypes 22F and 33F. This phase 3 study compared safety and immunogenicity of V114 and PCV13 in infants.

Methods: A total of 1720 healthy infants 6 to 12 weeks of age were randomized 1:1 to receive a 4-dose regimen of V114 or PCV13. Safety was evaluated as the proportion of participants with adverse events (AEs). Serotype-specific immunoglobulin G (IgG) and opsonophagocytic activity (OPA) responses were measured 1month post-dose 3 (PD3), pre-dose 4-, and 1-month post-dose 4 (PD4).

Results: The proportion, nature, maximum intensity, and duration of injection-site, systemic, and serious AEs were generally comparable between recipients of V114 and PCV13. No serious AEs were reported to be vaccine related. In comparison to PCV13, V114 met non-inferiority criteria for all 15 serotypes based on IgG response rates at PD3. V114 further met non-inferiority criteria based on IgG GMCs for all serotypes at PD3 and PD4 except serotype 6A at PD3. V114-induced antibodies displayed functional activity as assessed by OPA.

Conclusions: In healthy infants, V114 has an acceptable safety profile and generates comparable quantitative and qualitative immune responses to the 13 serotypes shared with PCV13, with higher responses to serotypes unique to V114. These results support use of V114 in infant immunization.

Poster 16

Title: LONGITUDINAL ASSESSMENT OF NATURAL INFECTION AND VACCINE INDUCED SARS-COV-2 SPECIFIC IgG IN LONG-TERM CARE FACILITY RESIDENT

Authors: S. Oldford[1,2], P. Zanello[1], A. Sagan[1], M. Qurashi[1], C. O'Reilly[1], C. Arnold[3], K. Nakka[3], M. Pelchat[3], M-A. L'Anglois[3], L. MacDonald[2], S. Fraser[2], B. Goodall[2], A. Falkenham[1], B. Clarke[1], S. Searle[1], M. Andrew[1], S. McNeil[1], L. Barrett[1,2]

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Introduction: Elderly long-term care facility (LTCF) residents have been disproportionately affected by COVID-19 and have suffered significant mortality and morbidity. Correlates of immunologic protection and susceptibility are not defined in highly vulnerable, advanced age, cohorted populations such as in LTCF. Elderly individuals are also often co-infected with cytomegalovirus (CMV), which may impact SARS-CoV-2 immunity. Objective: To examine SARS-CoV-2 IgG antibody immunity in highly exposed uninfected and SARS-CoV-2 infected LTCF residents following natural infection/exposure and vaccination with COVID-19 mRNA vaccine, in the context of CMV co-infection and clinical characteristics.

Methods: During a COVID-19 outbreak at a local LTCF, peripheral blood was collected at baseline and 1 month from 108 residents, following informed consent. Plasma was isolated and anti-SARS-CoV-2 Spike, RBD and NP IgG antibodies were measured by automated ELISA. CMV co-infection was determined by ELISA using CMV-AD169 infected MRC-5 fibroblast cell line lysate. An 8-month follow-up sample was collected from 53/108 individuals and samples were collected from 44/108 individuals post 2 dose vaccination with mRNA vaccine.

Results: The cohort consists of highly exposed uninfected (n=48) and COVID-19 infected (n=60) LTCF residents. Between baseline and 1 month, 11/48 highly exposed individuals became COVID-19 infected. 72% of individuals were co-infected with CMV but there was no difference in CMV coinfection between highly exposed COVID-19 negative and COVID-19 infected individuals. Antibody levels did not significantly increase with time from infection and significantly declined by 8 months in the majority of COVID-19 recovered individuals (Spike: p=<0.0001; RBD: p=0.0009; NP: p<0.0001). Within COVID-19+ individuals, antibody levels were not associated with CMV co-infection, age, BMI, presence of co-morbidities or clinical frailty score at the time of enrollment. COVID-19 recovered individuals had significantly higher post-vaccination anti-Spike and anti-RBD IgG (both p<0.0001) than highly exposed but uninfected individuals.

Conclusions: These data demonstrate the lack of sustained IgG antibody response following COVID-19 infection in LTCF and poor vaccine induced immunity following two doses of mRNA vaccine in COVID naïve LTCF residents. These data support additional boosters for vulnerable LTCF residents and ongoing studies will assess the longevity of IgG levels following a third vaccine dose in LTCF residents.

Poster 17

Title: THE IMPACT OF FRAILTY ON MORTALITY AND ICU ADMISSION AMONG ADULTS HOSPITALIZED WITH SARS-CoV-2 INFECTION DURING THE PRE-VACCINATION ERA OF THE COVID-19 PANDEMIC IN CANADA

Authors: Mulpuru S, Andrew MK, Mackinnon-Cameron D, Luo J, Ambrose A, Ye L, Wilson K, Kuokam Lowe W, McNeil SA

Affiliation: Serious Outcomes Surveillance (SOS) Network, Canadian Immunization Research Network (CIRN), Canadian Center for Vaccinology (CCfV), Dalhousie University, Ottawa Hospital Research Institute

Introduction: Prognostic models for survival among patients with COVID-19 in Canada have not included frailty as an important risk factor. The objective of this study is to evaluate the association between progressive frailty and mortality and ICU admission, in the context of increasing age and medical comorbidity among hospitalized adults with COVID-19 in the pre-vaccination era in Canada.

Methods: We conducted a prospective cohort study among Canadian adults who were hospitalized with SARS-CoV-2 (COVID-19) infection between March 1st, 2020 and March 31st, 2021. We used the Serious Outcomes Surveillance (SOS) Network's infrastructure in acute care hospitals in Ontario, Quebec, Nova Scotia, and Alberta. The primary exposure was the degree of frailty among hospitalized adults, measured at the bedside with the validated Clinical Frailty Scale. We also collected patient-level demographics, comorbidities, and place of dwelling. The primary outcomes were death in hospital, and admission to the intensive care unit (ICU). We used multivariate logistic regression to examine the association between frailty and outcomes, after adjustment for prognostic covariates including age and cardio-pulmonary comorbidity.

Results: Among 3245 hospitalized adults with COVID-19, 62.4% (2025/3245) were >=65 years of age, while 31.4% (1020/3245) were >80 years. Bedside frailty assessments using the CFS found 41.4% (1343/3245) to be *Non-Frail*, 18.5% (599/3245) to be *Vulnerable*, 28.8% (933/3245) to be *Mildly Frail or Moderately Frail*, and 10.4% (337/3245) to be *Severe, Very Severe or Terminally Ill*. In-hospital mortality was 13% (423/3245), while 23.2% (752/3245) individuals were admitted to the intensive care unit. After adjustment for age, sex, and comorbidity, progressive degrees of frailty were associated with greater odds of death in a non-ICU setting; *Pre-Frail* (OR 4.1, 95% CI 2.1-7.9), *Frail* (OR 8.5, 95% CI 4.6-15.6), *Most Frail* (OR 22.9, 95% CI 12.2-43.1). After adjustment for age, sex, dwelling, smoking and comorbidity, *Pre-Frail* status was associated with greatest risk of ICU admission (OR 1.3, 95%CI 1.0-1.6), while *Frail* and *Most Frail* were associated with reduced ICU admission (OR 0.6, 95% CI 0.5-0.9; OR 0.2, 95% CI 0.1-0.4).

Conclusions: In the pre-vaccination era of the COVID-19 pandemic in Canada, frailty was a strong predictor of mortality in hospital, but not for ICU admission, after adjustment for age and comorbidity. Notably, even *Pre-Frail* status was highly associated with death, suggesting that frailty measurements should be considered as an important prognostic factor in the evaluation of hospitalized adults with COVID-19.

Poster 18

Title: THE FIRST CASE OF HUMAN *BABESIA MICROTI* INFECTION ACQUIRED IN ATLANITIC CANADA

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Introduction: Babesiosis is an emerging infectious disease caused by Babesia, a zoonotic hemoprotozoan parasite, with human disease in North America primarily attributed to Babesia microti. Clinical features range from asymptomatic infection to severe disease, and even death. To date, only rare cases of locally-acquired human babesiosis have been described from Central and Western Canada. This report describes the first case of B. microti acquired in Atlantic Canada.

Methods: A 58-year-old immunocompetent male presented in July 2021 at a southwest Nova Scotia hospital with history of a headache, photophobia, fatigue, weakness, and fevers. He denied recent travel or tick bites. Since 2019, he has received 3 courses of doxycycline for Lyme disease. Initial investigations revealed a normal white blood cell count, hemoglobin, and low platelets. Wright-stained peripheral blood smears to investigate his new onset thrombocytopenia, revealed intra-erythrocytic ring forms and extracellular merozoites suspicious for parasitic infection. Parasitemia was estimated at 2.3%. The National Microbiology Laboratory confirmed Babesia microti on whole-blood PCR. Clinical improvement was seen after starting treatment with 10 days atovaquone and azithromycin and 14 days doxycycline for possible Lyme co-infection. Parasitemia became undetectable by day 7.

Results: In Nova Scotia, the B. microti reservoir white-footed mouse and vector Ixodes scapularis is the same as for Borrelia burgdorferi, the causative agent of Lyme disease which is endemic in the province. Seroprevalence studies from the Canadian Blood Services found rare human cases of B. microti, and other surveillance studies identified B. microti-infected Ixodes ticks and animals in Manitoba, Ontario, Quebec, New Brunswick, and Nova Scotia.

Conclusions: We report the first confirmed locally-acquired B. microti infection in Atlantic Canada. Surveillance and healthcare provider education is required as epidemiology of tick-borne diseases changes in Canada.