20th Annual Infectious Diseases Research Day

&

7th Annual Canadian Center for Vaccinology Symposium

April 27 & 28, 2015

Halifax

Sponsored by

Canadian Center for Vaccinology

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

Dalhousie Infectious Diseases Research Alliance

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Welcome

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

Scott Halperin MD,FRCPC
Director
Canadian Center for Vaccinology

Welcome to the 20th Annual Infectious Diseases Research Day and 7th Annual CCfV Symposium

Our program this year is again filled with a variety of presentations and posters, from basic science to public opinion surveys. The study of infectious diseases and vaccines requires a spectrum of research skills to examine the microbes that cause disease, the biotechnology to prevent disease, and the behaviour needed to implement proven strategies. All of this research is interrelated and necessary to provide the evidence that will lead to improved health outcomes.

Research is conducted by experienced investigators working with highly qualified graduate and post graduate trainees, as well as skilled technicians, analysts and support staff, to ensure their research is developed and executed at the highest standards. Peer review is essential to this process, which is another reason we provide this annual opportunity to showcase local research to peers and the public. Your 'peer' evaluation is important, so when you receive an email later this week requesting your evaluation of these sessions, please give us your feedback so we can continue to improve this learning experience for everyone.

We know that these two half days will be filled with excellent presentations from local and international experts, and hope that you will take advantage of this exposure to new and exciting research. Ask questions, talk with colleagues, and learn as much as you can about the process and results of research.

On behalf of all of you, we thank the dedicated planning committee and the financial support from our corporate sponsors which makes this educational opportunity possible.

With thanks to….

This program is supported in part by educational grants provided by:

The Planning Committee

Joanne Langley, Chair
Mary Appleton
Susan Brushett
Glenn Campbell
Michael Fleming
Shelly McNeil
Audrey Steenbeek
Allison Young

Program

Monday April 27		
1:00 – 2:00pm	Presentation: Tom Clark MD *Ebola Vaccines: Evaluation in the Midst of an Epidemic*	IWK Health Centre O.E. Smith auditorium
2:00 – 2:30pm	Presentation: Karina Top MD *A global perspective on adverse event surveillance in maternal immunization programs*	
2:30 – 3:00pm	Presentation: Donna MacDougall PhD *Condition of Service Influenza Prevention Policies*	
3:00 – 4:30pm	Poster judging (posters on display 1:00 – 5:30)	IWK Health Centre Gallery
4:30 – 5:30pm	Panel discussion: *Answering the tough questions about vaccines* Tom Clark MD, Scott Halperin MD, Kim McGill RN BScN, Rob Strang MD *Moderator* Joanne Langley MD	IWK Health Centre O.E. Smith auditorium
Tuesday April 28		
8:00 – 9:00am	TJ Marrie Lecture (Grand Rounds): Robert Fowler MD *The Lessons of Ebola*	Halifax Infirmary RB Theatre
9:20 – 12:30pm	Oral Presentations (10)	
12:30 – 2:00pm	Buffet lunch and presentation: Joni Guptill MD *MSF/Doctors without Borders: Ebola in West Africa- An Unprecedented Outbreak*	

Speakers

Thomas A. Clark MD, MPH
Supervisory Medical Officer
Centers for Disease Control and Prevention, Atlanta

Dr. Clark has worked at the Centers for Disease Control and Prevention for 14 years, beginning his CDC career as a "Disease Detective" in the Epidemic Intelligence Service program. He served as Epidemiology Team Lead and subsequently as Acting Chief of the Meningitis and Vaccine Preventable Diseases Branch, leading laboratory and epidemiologic investigations and policy development for pertussis, meningitis, and other bacterial vaccine-preventable diseases. He and his team played a key role in the successful implementation and evaluation of MenAfriVac—a novel, low-cost conjugate vaccine developed to end epidemic meningitis in sub-Saharan Africa. He also led efforts to use a novel but unlicensed meningitis B vaccine in response to simultaneous outbreaks on two college campuses. More recently, he led development of a plan to evaluate candidate Ebola vaccines in the ongoing epidemic in West Africa. He has published over 75 peer-reviewed and scientific papers and book chapters.

Robert Fowler MD, MDCM, MSc
Senior Scientist, Evaluative Clinical Sciences, Trauma, Emergency & Critical Care Research Program, Sunnybrook Research Institute
Physician, Sunnybrook Health Sciences Centre
Associate professor, Department of Medicine and Interdepartmental Division of Critical Care Medicine, University of Toronto

Dr. Fowler is a clinician, teacher and supervisor for medical students, residents and clinical fellows. He also has an active research program focused upon clinical outcomes of critically ill patients. He has published many research papers and holds a number of peer-reviewed grants in support of his academic work.

Karina Top MD, MSc
Assistant Professor, Pediatrics and Community Health & Epidemiology, Dalhousie University
Investigator, Canadian Center for Vaccinology

Dr. Top is co-principal investigator of the Special Immunization Clinic Network in the Canadian Immunization Research Network and co-Investigator with the Canadian Immunization Monitoring Program Active. Her research interests include vaccine safety surveillance, clinical management of patients after an adverse event following immunization and vaccine safety in patients with chronic medical conditions.

Donna MacDougall BScN, MSc, PhD
Associate Professor, School of Nursing
St. Francis Xavier University, Antigonish
Investigator, Canadian Center for Vaccinology

Dr. MacDougall's post-doctoral work at Dalhousie University focused on the impact of a universal rotavirus vaccine program using different delivery models. Additional research centers on vaccine decision-making, vaccination education, and health policy research including the synthesis, dissemination and exchange of knowledge using a variety of social media platforms. Her most recent research includes examining the impact of the BC influenza prevention policy on immunization rates in healthcare workers, the perspectives of Ontario parents regarding influenza immunization in school-based immunization programs, NS condition of service influenza policy study, and Tdap vaccine for adults. She is also on the Pharmacists as Immunizers (PAI) research team, exploring the role of pharmacists as immunizers and their impact on immunization rates and disease prevention in the Maritimes.

Joni Guptill MD
Dr. Guptill has been involved with Doctors without Borders for more than twenty years. She completed studies in Tropical Medicine in London England in 1990 and while in London was recruited by Doctors without Borders. She opened the Atlantic Canada office for MSF in 1990 and over the last 25 years has been involved in many capacities including overseas projects in Somalia, Turkey, China, Syria/Iraq, and South Sudan. In 2006 she joined the Board of MSF Canada and served for 6 years as an active member. She acted as President of the Board between 2009 and 2011.

Poster Presentations

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

Oral Presentations

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

Abstracts

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

1. HANSEN'S DISEASE IN A NONIMMIGRANT CANADIAN WITHOUT TRAVEL OUTSIDE OF NORTH AMERICA

AUTHORS: P. Bonnar, I. Davis

AFFILIATION: Dalhousie University

Introduction:
Mr. BR is a 69-year-old man from Atlantic Canada who presented with a ten-month history of rash. It was described as macular and erythematous. The rash started on his right thigh but subsequently spread to involve his torso (anterior and posterior) and all of his limbs. The skin lesions were not pruritic, warm, tender, or associated with sensation changes. There was no temporal relation with change in medications, lotions, cleaning supplies, or detergents.

He had no infectious contacts with skin lesions or systemic illnesses. There were no recent hospitalizations or history of dermatologic illnesses. Mr. BR had no systemic symptoms of fever, night sweats, or weight loss. He did not notice any lymphadenopathy. On review of symptoms, he had no weakness, blurred vision, cranial nerve symptoms, dyspnea, chest pain, bowel or urinary changes.

A punch biopsy showed superficial and deep perivascular lymphohistiocytic infiltrate with foamy cytoplasm. A Fite stain revealed abundant and focally clumped acid-fast organisms within the foamy histiocytes. Real time PCR from skin biopsy tissue confirmed *Mycobacterium leprae* by 16S rRNA gene sequencing analysis.

Conclusions:
Hansen's disease (HD) is rare in Canada. In 2012, seven cases were reported to the Public Health Agency of Canada. This rate of 0.02 per 100,000 has been stable since the late 1990s. However, autochthonous leprosy has not been reported in Canada. This case describes an unlikely presentation of HD: a nonimmigrant Canadian without travel outside of North America. Similar cases have been described in the southern United States and may be secondary to exposure to the nine-banded armadillo (*Dasypus novemcinctus*). This animal is the only known nonhuman, natural occurring *M. leprae* host. The strain of *M. leprae* in wild armadillos is the same as that found in many North American humans. This case highlights the possibility of HD acquired within North America without an obvious exposure and should be considered for chronic rashes without a clear, alternative diagnosis and not responding to usual treatment.

2. THE NONCLINICAL PATH TO PHASE 1 CLINICAL TESTING OF DPX-RSV(A)

AUTHORS: Lisa MacDonald[†], Marianne Stanford[†*], Alecia MacKay[†], Valarmathy Kaliaperumal[†], Nicholas Bartlett[†], Andrea West[†], Andrea Penwell[†], Rajkannan Rajagopalan[†], Leeladhar Sammatur[†], Joanne Langley[*], Marc Mansour[†*]

AFFILIATION: Immunovaccine, Inc.[†] and the Canadian Centre for Vaccinology[*], Halifax, NS, Canada

Introduction:
The development of a vaccine to RSV has been hampered by the fact that natural infection fails to provide protection against subsequent infection. Targeting the Short Hydrophobic (SH) protein of RSV, targets the infected cell instead of the RSV virion. A 23 aa portion of the ectodomain of SH protein (SHe) from RSV strain A has been formulated in DepoVax™, a novel adjuvanting vaccine formulation that provides controlled and prolonged exposure of antigens plus adjuvant to the immune system, resulting in a strong, specific and sustained immune response.

Methods:
The SHe peptide was formulated in DepoVax (DPX-RSV(A)) and administered to mice for the assessment of immunogenicity of the antigen. Antigen-specific antibodies were measured by ELISA. Rats were used as the model animal for GLP safety and toxicology testing of the intended clinical formulation.

Results:
Studies in mice have confirmed an increase in immunogenicity of SHe antigen after formulation in DepoVax; a dose response trend was observed and all components of the DepoVax formulation were demonstrated to be required for optimal immunogenicity. GLP testing of the clinical formulation demonstrated that the vaccine was well tolerated.

Conclusions:
A Clinical Trial Application for the clinical testing of DPX-RSV(A) was successfully submitted to Health Canada and phase 1 clinical testing of this novel RSV vaccine. Manufacture of the vaccine is underway and the study will be initiated in the first half of 2015.

3. ENUMERATION OF STRESSED LISTERIA MONOCYTOGENES FROM READY-TO-EAT FROZEN FOOD PRODUCTS

AUTHORS: J. McLennon, A. Borza, M. Mosher, R. Garduno

AFFILIATION: Canadian Food Inspection Agency, Government of Canada

Introduction:
Canadian Food Inspection Agency (CFIA) microbiology testing laboratories currently use the Health Canada (HC) compendium method MFLP-74 to enumerate *Listeria monocytogenes* in foods. The regulatory limit or action level for *L. monocytogenes* is set by HC at 100CFU/g of food. Processing treatments, including exposure to heating and freezing are known to induce cell injury or stress. For *L. monocytogenes*, this stress may cause sensitivity to selective agents found in microbiological media. MFLP-74 does not include a step for cellular resuscitation as do other international reference methods. Here, we evaluated a thin agar layer (TAL) method as a means to improve cellular resuscitation and recovery of stressed *L. monocytogenes* from frozen food products.

Methods:
MFLP-74 and the TAL method were used to enumerate cold injured (-20°C freezer for 2 h, then room temperature (RT) for 2 h) *L. monocytogenes* from frozen vegetables, as well as heat-stressed (55ºC for 39 min) *L. monocytogenes* from frozen seafood products, and frozen heat-processed meat products. The method involves overlaying 14 mL of nonselective solid medium (Tryptic Soy Agar, TSA) onto plates of the selective agars Oxford (OXF) and Rapid'L mono (RLM). The microbial recovery from OXF and RLM alone was compared with the recovery from the overlaid selective agars (OXF-TSA, RLM-TSA).

Results:
The main evaluation criterion was agreement between count results obtained by the two methods. The study found a significant difference ($p<0.05$) between MFLP-74 (using RLM and OXF), and the TAL method (using RLM-TSA and OXF-TSA) for each food type. The TAL method recovered a higher number of cells than MFLP-74. When the four agar types were directly compared to each other, counts were significantly different ($p<0.05$) except for RLM vs. OXF-TSA, which showed no significant difference.

Conclusions:
The TAL method demonstrated superior recovery capacity than selective media alone to enumerate stressed *L. monocytogenes* from frozen foods, including products contaminated with *L. monocytogenes* near the action level of 100 CFU/g. The use of the TAL method in routine testing would thus provide a more accurate evaluation of *L. monocytogenes* levels in frozen products.

4. VALIDATION OF HEMAGGLUTINATION INHIBITION ASSAY FOR ASSESSING IMMUNOGENICITY OF INFLUENZA VACCINES OR FOLLOWING INFLUENZA INFECTION

AUTHORS: M Warhuus[1], M Zacour[2], P Tang[3], G Boivin[4], Y Li[5], B Ward[6], M ElSherif[1], Hatchette TF[1]

AFFILIATION: [1]Canadian Center for Vaccinology, Dalhousie, Halifax, NS; [2]PCIRN Montreal; [3]BC-CDC, Vancouver BC; [4]Laval, Quebec City, PQ; [5]NML, Winnipeg, MB; [6]McGill, Montreal, PQ

Introduction:
Quality assurance is a fundamental component of a quality laboratory system. The hemagglutination inhibition (HAI) assay, the 'gold standard' for influenza serology, adds multiple challenges for standardization. The PCIRN/CIRN reference laboratory network has standardized protocols, performed quality assurance testing, and have examining sources of variance between laboratories to maximize the best possible comparability between laboratories. In this project we wanted to determine if HAI results from different laboratories using a standardized panel to evaluate assay precision, reproducibility and accuracy between the different PCIRN/CIRN laboratories fall within an acceptable range.

Methods:
Following the same procedure, one operator at five PCIRN/CIRN sites [BCCDC (Tang); NML (Li); McGill (Ward); Laval (Boivin); Dalhousie (Hatchette)] tested a blinded panel of 10 sera per virus over six separate runs over three different days to evaluate intra-laboratory and inter-laboratory variations in HAI titres against two influenza viruses, pH1N1 (A/California like) and H3N2 (A/Perth like). The 20 sera were chosen and exchanged based on known titres spanning high, low, and negative readings. Results from all sites were compiled and analyzed collectively as a single data set.

Results:
HAI titres were compared within a lab, and between labs. The "true result "was considered the NML titre. Dilutions less than 4 fold of the true value were considered within acceptable assay error. A titre of 1/40 was considered protective. In Halifax, there was a 100% intra-assay precision (repeatability), assessed by duplicate testing of samples in each run. Reproducibility or inter-assay precision was also 100% given that replica from all samples were with 1 twofold dilution. The median %CV between samples over different runs was 22.7 (0-43). With 9 out of the 10 specimens within 1 twofold titter of other laboratories, Halifax's accuracy was 90% with H1N1, compared to 100% with H3N2.When all the labs were compared against NML, accuracy was 80% for H1N1, 100% for H3N2, and 90% for all viruses.

Conclusions:
The HAI assay has shown equivalent performance across PCIRN/CIRN reference centers. This validation should satisfy regulatory requirements when HAI is used to evaluate the immunogenicity of influenza vaccines and/or adjuvants in humans.

5. INFLUENZA AND OTHER RESPIRATORY VIRUS CO-INFECTIONS AMONG HOSPITALIZED ADULTS IN CANADA

AUTHORS: **M Petten[1]**, A Oliver[1], CS MacRae[1], S McNeil[1,2], M ElSherif[1], V Shinde[4],D MacKinnon-Cameron[1], L Ye[1], A Ambrose[1], J Leblanc[1,3], A McGeer[5], TF Hatchette[1,3] on behalf of the Public Health Agency of Canada/Canadian Institutes of Health Research Influenza Research Network (PCIRN) Serious Outcomes Surveillance (SOS) Network Investigators and the Toronto Invasive Bacterial Diseases Network (TIBDN)

AFFILIATION: [1]Canadian Center for Vaccinology, IWK Health Centre and Capital Health, Dalhousie University, [2]Division of Infectious Diseases, [3]Department of Medicine, Capital Health, [3]Department of Pathology and Laboratory Medicine, Capital Health, [4]GlaxoSmithKline Biologicals, [5]Mount Sinai Hospital, Toronto, Ontario

Introduction:
The aim of this study was to identify viral co-infections in hospitalized adults with acute respiratory disease, using multiplex-PCR, and describe the presenting features and clinical outcomes.

Methods:
From November 2011 - May 2012, the PCIRN SOS Network conducted active surveillance for influenza among hospitalized adults in 40 acute care facilities in 5 provinces across Canada. A nasopharyngeal swab for influenza reverse transcriptase polymerase chain reaction (RT-PCR) was obtained from all admitted patients meeting study criteria. Specimens testing positive for influenza were tested for the presence of parainfluenza virus, adenovirus, respiratory syncytial virus (RSV), human metapneumovirus (hMPV), coronavirus and rhinovirus using the Seeplex®eRV15 assay. Clinical features and outcomes were compared between those with influenza and those with influenza co-infected with other respiratory viruses.

Results:
1213 patients were tested for influenza, of these 446 (37%) were positive. Respiratory viral co-infections were found in 24 (5%) of the influenza positive patients. The mean age of patients with influenza only was 67years, whereas the age of patients with influenza and a viral co-infection was slightly higher at 70years. Parainfluenza (10 cases) and Coronavirus (8 cases) were the most common co-infections. Only 40% of patients with influenza and parainfluenza had received an influenza vaccine, which was comparable with the uptake in the influenza only group (47%). There were two deaths in the influenza co-infection group, both due to influenza B with coronavirus co-infection. No patient with influenza and a co-infection was admitted to the ICU.

Conclusions:
The severity and outcome of disease caused by influenza was not significantly modified when a co-infection was present. This study was limited by the available sample size; further research is needed. The PCIRN SOS Network is critical for ongoing assessment of the burden of respiratory viral diseases in addition to its importance for epidemic or pandemic preparedness.

6. FRAILTY IN RELATION TO INFLUENZA BURDEN OF DISEASE AND SERIOUS OUTCOMES: A REPORT FROM THE PCIRN SERIOUS OUTCOMES SURVEILLANCE NETWORK

AUTHORS: E MacDonald, S McNeil, A McGeer, J McElhaney, J Johnstone, V Shinde, D MacKinnon-Cameron, L Ye, A Ambrose and M Andrew on behalf of the Public Health Agency of Canada/Canadian Institutes of Health Research (PCIRN) Serious Outcomes Surveillance (SOS) Network Investigators and the Toronto Invasive Bacterial Diseases Network (TIBDN) Investigators

Introduction:
Frailty is strongly associated with health outcomes in older adults. Nevertheless, its importance in relation to influenza burden of disease remains incompletely understood. We sought to investigate frailty relative to influenza vaccination rates, burden of disease by influenza strain, and outcomes in hospitalized older Canadians, and to compare the influence of frailty with age.

Methods:
In the 2011–12 influenza season, the Serious Outcomes Surveillance Network undertook active surveillance for influenza-like-illness requiring acute care admission in 40 Canadian hospitals. Clinical data collection for patients aged 65+ included a frailty index (FI), a well validated measure of health and functional status. To allow comparison across grades of frailty, the FI was categorized into low, medium and high frailty. Nasopharyngeal swabs were obtained for all enrolled participants; those testing positive for influenza were typed for strain using PCR. In this report, outcomes were reported at 30 days post hospital discharge.

Results:
346 older adults aged 65+ had lab-confirmed influenza, of whom 237 (68.5%) were aged 75+. Influenza vaccination rates increased with increasing frailty from 48.9% in the least frail to 71.4% in the most. A similar but less pronounced trend was seen by age (53.2% for ages 65-75 and 57.8% for those 75+). The burden of influenza B increased with frailty (55.5% of the least frail and 71.4% of the most frail) and with age (44.9% for 65-75 and 59.9% for 75+). Outcomes worsened with increasing frailty and age: mortality was 5.5% among the least frail vs. 35.7% in the most frail, and 5.5% for ages 65-75 vs. 15.2% for 75+.

Conclusions:
Increasing frailty was associated with higher influenza vaccination rates, increasing burden of influenza B, and with serious outcomes. Frailty enriches our understanding of influenza burden in older adults and should be considered in future studies.

7. CARDIAC COMPLICATIONS OF COMMUNITY ACQUIRED PNEUMONIA AMONGST HOSPITALIZED CANADIAN ADULTS: A PUBLIC HEALTH AGENCY OF CANADA/CANADIAN INSTITUTES OF HEALTH RESEARCH (PCIRN) SERIOUS OUTCOMES SURVEILLANCE NETWORK STUDY

AUTHORS: G Worthen[1], A Ambrose[1], M Andrew[1,2], G Boivin[3,4], W Bowie[5], M Elsherif[1], K Green[6], T Hatchette[1], J Johnstone[6], J Leblanc[1], M Loeb[7], D Mackinnon-Cameron[1], T Marrie, MD[2], A McCarthy[8], A McGeer[6], M Semret[9], G Stiver[5], S Trottier[3], L Valiquette[10], D Webster[11], L Ye[1,] S McNeil[1] on behalf of the Public Health Agency of Canada/Canadian Institutes of Health Research Influenza Research Network (PCIRN) Serious Outcomes Surveillance Network Investigators

[1]Canadian Center for Vaccinology, IWK Health Centre and Capital Health, Dalhousie University, Halifax, NS, [2]Faculty of Medicine, Dalhousie University, Halifax, NS, [3]Centre Hospitalier Universitaire de Québec, Quebec, QC, [4]Laval University, Quebec, QC, [5]University of British Columbia, Vancouver, BC, [6]Mount Sinai Hospital, Toronto, ON, [7]McMaster University, Hamilton, ON, Faculty of Medicine, Dalhousie University, Halifax, NS, [8]Ottawa Hospital General Campus, Ottawa, ON, [9]McGill University, Montreal, QC, [10]Université de Sherbrooke, Sherbrooke, QC, [11]Horizon Health, St. John, NB

Introduction:
Community acquired pneumonia (CAP) is an important contributor to morbidity and mortality among Canadian adults. CAP can precipitate acute cardiac events. We sought to characterize the incidence, risk factors and outcomes of cardiac complications among Canadian adults hospitalized with CAP and to evaluate the effectiveness of pneumococcal immunization in the prevention of these complications.

Methods:
The PCIRN Serious Outcomes Surveillance (SOS) Network conducted active surveillance for CAP in 9 SOS Network sites from 12/1/10 to 12/31/13. Surveillance monitors reviewed hospitalizations daily and enrolled consenting adults admitted with CAP. Detailed information regarding comorbidities, hospital course and outcomes were collected. In-hospital occurrence of unstable angina (UA), myocardial infarction (MI), incident congestive heart failure (CHF), and incident arrhythmias were recorded. Vaccine effectiveness was estimated as 1-OR of pneumococcal vaccination in CAP patients with cardiac complications compared to those without.

Results:
6833 cases of CAP were enrolled; 706 (10.3%) experienced a cardiac complication in hospital: 384 (5.6%) arrhythmia, 211 (3.1%) CHF, 178 (2.6%) MI, and 22 (0.3%) UA. Patients with cardiac complications were older (mean age 75.7y vs 68.4y; p=0.000) and were more likely to have underlying comorbidities (94.6% vs 92.0%; p=0.01) and were more likely to require ICU admission (36.4% vs 16.1%; p=0.000) and mechanical ventilation (23.7% vs 10.1%; p=0.000), had longer length of stay (median 11d vs 7d; p 0.000), and were more likely to die (25.2% vs 10.4%; p=0.000). Overall adjusted effectiveness of pneumococcal vaccine in the prevention of cardiac complications was 19% (3% - 32%).

Conclusions:
Cardiac complications are common amongst adults admitted with CAP and are associated with increased morbidity, mortality, and healthcare utilization. Pneumococcal vaccination is associated with a reduced risk of cardiac complications. Evaluation of cost-effectiveness of immunization programs should address this. Improved prevention of pneumococcal disease may result in significant cost savings.

8. CHARACTERIZATION OF ANTIGEN-TARGETING FUSION PROTEINS FROM *ESCHERICHIA COLI*

AUTHORS: Yunnuo Shi, Scott A. Halperin, and Song F. Lee

AFFILIATION: Department of Microbiology and Immunology, Dalhousie University; Canadian Center for Vaccinology, IWK Health Centre

Introduction:
A *Streptococcus gordonii* based oral mucosal vaccine is an attractive vaccination strategy. However, the sub-optimal immune response induced by recombinant *S. gordonii* in the oral cavity is a major obstacle to vaccine development. Antigens delivered by coupled molecules specific for receptors on antigen-presenting cells can enhance immune responses. As a first step in using the antigen-targeting approach in *S. gordonii*, an antigen-targeting fusion protein consisted of the C-terminal fragment of ovalbumin (OVA) fused to the extracytoplasmic region of CD40 ligand (CD40LS) was constructed and produced in *Eschericia coli*. The ability of the OVA fusion protein to bind to human CD40 was examined.

Methods:
The DNA coding for OVA-CD40LS was constructed by ligating the DNA coding for OVA to that coding for CD40LS, both obtained by polymerase chain reaction. The fusion protein DNA was then cloned into the plasmid pComb3X and transformed into *E. coli* for protein expression. A mutant OVA fusion protein with a deletion of 5 amino acids of the CD40L-binding region (OVA-ΔCD40LS) was also constructed as a control. Protein production was detected by Western blotting. Periplasmic extracts and cell lysates were prepared from *E. coli* and used for protein purification by nickel affinity chromatography. The fusion proteins were quantified, standardized by densitometry, and tested for binding to human CD40 (hCD40) by ELISA.

Results:
Western blotting showed that *E. coli* carrying the fusion constructs produced a 31kDa protein that was recognized by the anti-OVA and anti-hCD40L antibodies, which was absent in *E. coli* not carrying the fusion constructs. These results suggest that the OVA fusion proteins have been successfully constructed and expressed by *E. coli*. The fusion proteins were partly purified from *E. coli* cell lysates using a His60 Ni gravity column. OVA-CD40LS showed strong binding ability to human CD40 in ELISA, while the OVA-ΔCD40Ls showed weak binding.

Conclusions:
OVA-CD40LS showed the ability to bind to hCD40. The reduced binding ability of OVA-ΔCD40LS suggested that the binding observed with OVA-CD40LS was due to CD40LS-CD40 specific interaction. Further purification of the fusion proteins is required for *in vitro* and *in vivo* functionality test in future studies.

9. THE ROLE OF MAST CELLS IN *CHLAMYDIA* INFECTION

AUTHORS: E. Shantz[1], J. S. Marshall[1] and J. Wang[1,2,3]

AFFILIATION: [1]Department of Microbiology & Immunology, [2]Department of Pediatrics, Dalhousie University [3]Canadian Center for Vaccinology

Introduction:
Chlamydia is an intracellular bacterial pathogen that infects mucosal epithelial cells of the genital, respiratory and ocular tracts. *Chlamydia trachomatis (Ct)* is the most common bacterial STI in humans and the leading cause of infectious blindness, with over 100 million infections reported globally each year. Mast cells are critical sentinel immune cells located at tissues that interact with the external environment such as the skin, airways and reproductive tract. Although they are traditionally implicated in allergic responses, mast cells can be activated by pathogen recognition and other receptors to selectively release cytokine and chemokines that recruit immune effector cells. Although many innate and adaptive immune responses to *Ct* infection of the genital tract have been investigated, the role of mast cells remains unclear.

Methods:
Tissue sections of upper reproductive tracts harvested from mice three days post-infection with *Cm* were stained overnight with 0.5% toluidine blue to visualize mast cells. Bone marrow-derived murine mast cells (BMMCs) at a concentration of 2.0 x 10^6 cells/ml were incubated at 37°C with *Chlamydia muridarum (Cm)* at a multiplicity of infection (MOI) of 1 and 5. Incubation with Pam_3CSK_4 (10 µg/ml), peptidoglycan (50 µg/ml) and media only were used as controls. Supernatants were harvested at 24 and 48 hours. Pro-inflammatory cytokines, including IL-1β and IL-6, were measured by enzyme-linked immunosorbent assay (ELISA).

Results:
Mast cells were present in the myometrium and endometrium layers of the uterus at three days post-infection. At 24 hours, IL-1β and IL-6 were measurable in supernatants from BMMCs stimulated with both doses of *Cm*. At 48 hours, IL-6 was present at similar levels to the earlier time point but IL-1β levels were negligible or undetectable.

Conclusions:
These data demonstrate that mast cells are present in the genital tract at the site of *Cm* infection and are able to produce pro-inflammatory cytokines in response to *Cm*. This suggests that mast cells may have a role in immediate protection against *Cm* infection. Future studies using human cord blood-derived mast cells (CBMCs) and *Ct* will investigate this interaction in a human system. Furthermore, *in vivo* studies in mast cell-deficient and wild-type mice will provide insight into the role of mast cells within the overall immune response.

10. THE LEGIONELLA PNEUMOPHILA CHAPERONIN 60 (HTPB) INTERACTS WITH THE HUMAN HOMOLOG OF ECM29

AUTHORS: K. Valenzuela[1], J. Rohde[1], G. Moreno-Hagelsieb[2], R. Garduno[1].

AFFILIATION: 1-Dalhousie University, 2-Wilfrid Laurier University

Introduction:
Chaperonins are highly conserved housekeeping proteins that help other proteins to fold. The GroEL/GroES folding machinery of *E.coli* is formed by two GroEL heptameric rings that constitute the folding chamber and a GroES heptameric cap that keeps unfolded proteins inside the chamber. However, bacterial chaperonins also possess protein-folding independent functions acting as proteases, toxins or adhesins. Unlike GroEL, the *L. pneumophila* chaperonin (HtpB) reaches the cytoplasm of infected cells and also has been implicated in host cell invasion, mitochondria recruitment and cell signaling. We hypothesized that HtpB must interact with a cytoplasmic protein in the host cell to exert its unique functions and that this functional gain is due to substitutions in key amino acid positions.

Methods:
A Yeast two hybrid (Y2H) screening using a human library was performed to find interaction partners of HtpB. The interaction was confirmed by Co-Immunoprecipitation (Co-IP) in yeast. Identification of key amino acids possibly involved in the protein-folding independent functions of HtpB was carried out using a bioinformatics approach. The selected amino acids were mutated and then mutant versions of HtpB or GroEL were tested on their ability to interact with ECM29 by Y2H.

Results:
The human homolog of ECM29 interacts with HtpB but does not interact with GroEL. From the bioinformatics analysis, 10 amino acids that are different between HtpB and GroEL were selected to be mutated: M68, M212, S236, K298, N507 and a C-terminal fragment (residues 471 to 475). Single-residue mutations in the selected amino acids did not affect interaction of HtpB with ECM29; however, multi-site mutations on three or more residues diminished HtpB-ECM29 interaction. Importantly, GroEL acquired the ability to interact with ECM29 after mutation of the 10 selected amino acids to the corresponding HtpB residues.

Conclusions:
We identified a host cytoplasmic protein (ECM29) that interacts with HtpB. Using bioinformatics tools we were able to predict amino acids involved in the HtpB-ECM29 interaction and possibly in other folding-independent functions of HtpB. ECM29 couples the 26S proteasome to molecular motors, endocytic vesicles and the endoplasmic reticulum. Exploiting this interaction could be a yet undescribed strategy used by *L. pneumophila* to alter vesicular trafficking in the host cell.

11. THE HOST DEFENSE PEPTIDE, LACTOFERRICIN, AND ITS IMMUNOMODULATORY EFFECTS ON LPS-STIMULATED MACROPHAGES

AUTHORS: Alicia Malone, Laurence Madera, David Hoskin

AFFILIATION: Department of Microbiology and Immunology, Dalhousie University

Introduction:
Inflammation following injury or infection is a mechanism by which the body uses specialized immune cells, such as macrophages, to eliminate invading pathogens. However, when the infecting agent cannot be eradicated, inflammation can persist, leading to a variety of negative consequences for the host. Recently, it has been suggested that chronic inflammation caused by microbial infection can be treated by exploiting small cationic proteins, referred to as host defense peptides (HDPs), which exhibit immunoregulatory activities. In this study, we have investigated the effects of the HDP lactoferricin, on the function of LPS-stimulated macrophages.

Methods:
The effect of bovine, murine, and human lactoferricin on cytokine protein production and cytokine mRNA expression by mouse and human macrophages was measured by enzyme-linked immunosorbent assay (ELISA) and quantitative real-time polymerase chain reaction (qRT-PCR), respectively. Nitric oxide production by LPS-stimulated macrophages was measured via Griess assay. Activation of the NFκB pathway was demonstrated through immunofluorescence and western blotting for various mediators of the inflammatory signaling pathway.

Results:
Bovine and human lactoferricin significantly decreased the production of proinflammatory cytokines that are upregulated by LPS stimulation, including TNFα and IL-6. These changes may be due to the ability of lactoferricin to abrogate LPS-induced activation of the NFκB pathway, which was demonstrated through western blot and immunofluorescence assays. Interestingly, upregulation of the anti-inflammatory cytokine IL-10, along with increased phosphorylation of p38, is seen when macrophages are treated with peptide alone.

Conclusions:
Our findings suggestthat lactoferricin acts as an immunomodulatory agent that downregulates proinflammatory macrophage response to LPS. Lactoferricin also acts as a antiinflammatory mediator in the absence of LPS. Our findings suggest that lactoferricin may have potential for use in controling acute and chronic inflammation originating from bacterial infection.

12. ON THE HUNT FOR PEPTIDE ANTAGONISTS TARGETING CLOSTRIDIUM DIFFICILE TOXINS

AUTHORS: B.-L. Rooney[1,2], J.G LeBlanc[3], N. Thomas[2], J. LeBlanc[1,2]

AFFILIATION: Capital District Health Authority (CDHA)[1], Dalhousie University[2], Centro de Referencia para Lactobacilos (CERELA)[3]

Introduction:
C. difficle infection is a leading cause of nosocomial antibiotic-associated diarrhea. Though treatment is available, recurrent disease becomes a large burden to healthcare systems. Since pathogenesis is associated with two toxins, TcdA and TcdB, this study aimed to identify peptides that could neutralize the effects of these toxins.

Methods:
Three M13-phage display libraries (Ph.D.-7, 12, C7C) expressing peptides were tested against TcdA and TcdB toxins that were labeled at their terminus with a hexameric (His_6)-tag and purified from a *Bacillus megaterium* expression system. Briefly, each bacteriophage library expressing the various peptides was incubated in the presence of either His_6-tagged TcdA or TcdB that was immobilized onto nickel-nitrilotriacetic acid magnetic beads. Following several washes, the remaining phage bound to toxin were eluted with native toxin. After several biopanning steps with increasing amounts of native toxin, high affinity toxin-binding peptides were isolated. To evaluate whether the toxin-binding peptides could prevent the cytopathic effects (CPE) of TcdA and TcdB on cultured FSK and HT29 cells, a cell culture cytotoxicity neutralization assay (CCCNA) was performed. The assay was performed using toxins derived from wild-type *C. difficile* strain 630 or hypervirulent strain Nap1 or their toxin-deletion mutants (*tcdA+B-* or *tcdA-B+*). Similar CCCNA experiments were performed using synthetic decameric peptide libraries mimicking the TcdA or TcdB receptor-binding domain sequence composition.

Results:
Phage display experiments demonstrated that thousands of toxin-binding peptides could be isolated against TcdA and TcdB. However, to date, no peptide has been isolated that could neutralize the CPE of TcdA or TcdB on FSK or HT29 cells. In contrast, a synthetic peptide was able to prevent entry of TcdB at concentrations found in clinical specimens.

Conclusions:
This study suggests that toxin-binding properties of peptides may be insufficient to neutralize the CPE of *C. difficile* toxins, but peptides mimicking the amino acid composition of the receptor-binding domain may be a fruitful avenue of research. Further investigations are underway to identify peptides able to prevent CPE derived from TcdA and methods for peptide delivery.

13. IDENTIFICATION OF NOVEL PCR TARGETS FOR THE DISCRIMINATION OF VACCINE-PREVENTABLE SEROTYPES OF STREPTOCOCCUS PNEUMONIAE USING NEXT GENERATION SEQUENCING

AUTHORS: D. Gaston[1], I. Martin[2], T.F. Hatchette[1], S. McNeil[1] and J. LeBlanc[1], and on behalf of the Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS) Network Investigators

AFFILIATION: [1]Canadian Center for Vaccinology, IWK Health Centre and Capital Health, Dalhousie University, Halifax, NS, Canada; [2]Streptococcus and STI Unit, National Microbiology Laboratory, Public Health Agency of Canada, Winnipeg, MB, Canada.

Introduction:
S. pneumoniae is a major cause of morbidity and mortality. Since 2010, the CIRN SOS network has been using a PCR-based serotyping method to establish the burden of pneumococcal disease in Canadian adults. While the distribution of *S. pneumoniae* serotypes obtained with PCR mirrored trends obtained with traditional Quellung serotyping, PCR was unable to discriminate between some vaccine-preventable serotypes. This study aims to identify novel PCR targets using whole genome sequencing and comparative genomics to discriminate vaccine-preventable serotypes of *S. pneumoniae*.

Methods:
Whole genome sequencing was performed using Illumina MiSeq technology on select *S. pneumoniae* serotypes that were previously characterized by Quellung seroytping. *S. pneumoniae* isolates were selected based on serotypes covered by PCV13 and PPV23 vaccines that could not be differentiated using PCR (6A/6B, 7F/7A, 9V/9A, 18C/18F/18B/18A, 9N/9L, 11A/11D, 12F/12A/12B/44/46, 15B/15C, 22F/22A, and 33F/33A/37).

Results:
Genome assembly has been performed and comparative genomics are underway to identify genetic biomarkers that are unique for each vaccine-preventable serotype of *S. pneumoniae.*

Conclusions:
Accurate discrimination of pneumococcal serotypes is crucial to characterize *S. pneumoniae* epidemiology, determine the burden of pneumococcal disease, and evaluate the impact of pneumococcal vaccine programs. This study describes the development of genetic methods to accurately discriminate between vaccine-preventable serotypes of *S. pneumoniae* using PCRs. A PCR-based serotyping method that can accurately discriminate vaccine-preventable serotypes of *S. pneumoniae* could be used directly on clinical specimens, without culture of the organism, and thus providing a powerful tool for epidemiological analyses.

14. INHIBITORS OF EUKARYOTIC INITIATION FACTOR 4A BLOCK REPLICATION OF INFLUENZA A VIRUS

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(The author requested that this abstract not be published)

15. INTERFERON-OMEGA (IFN-ω) REGULATION AND EXPRESSION BY VIRUS-INFECTED MAST CELLS

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Introduction:
Mast cells are important immune sentinels during viral infections via production of a wide range of cytokines including IFNs. Human type I IFNs include IFN-α, -β, -κ, -ω and –ε. Type I IFN members have distinct roles, despite binding to a common receptor (IFNAR). In the current study we investigate the expression and regulation of the less studied IFN-ω during viral infection.

Methods:
Cord blood-derived mast cells (CBMC, n=5) were infected with the mucosal pathogen reovirus type 3 Dearing or stimulated with poly(I:C). The epithelial cell lines A549, Caco-2, and HeLa, primary fibroblasts and peripheral blood mononuclear cells (PBMC, n=2) were also examined. Supernatants were harvested 24 hours post infection for ELISA analysis. mRNA gene expression was analyzed by qPCR. In some experiments, antibody blockade of IFNAR was included.

Results:
Similar to IFN-α and –β, the IFN-ω gene was upregulated by both CBMC and PBMC in response to reovirus infection. In contrast, epithelial cells and fibroblasts showed a preferential, low level expression of IFN-β. Similar results were observed for poly(I:C) stimulation. CBMC were confirmed as an important source of IFN-ω protein by ELISA. IFNAR blockade on reovirus-infected CBMC decreased IFN-ω production.

Conclusions:
IFN-ω was selectively induced in viral-infected mast cells compared to epithelial cells and fibroblasts. This expression is regulated by type I IFN signaling. Mast cell-rich mucosal surfaces are the main point of entry for viruses into the body. Our results show that mast cells, unlike epithelial cells, are an important source of diverse type I IFNs, including IFN-ω which in turn could induce an antiviral state in neighbouring epithelial cells to avoid virus propagation.

16. FUNCTIONAL ANALYSIS OF TWO PUTATIVE THIOL-DISULFIDE OXIDOREDUCTASES AND ASSOCIATED CCDA PROTEINS IN *STREPTOCOCCUS GORDONII*

AUTHORS: Naif A. Jalal, Lauren Davey, Scott A. Halperin, Song F. Lee

AFFILIATION: Department of Microbiology and Immunology, Dalhousie University; Canadian Center for Vaccinology, IWK Health Center

Introduction:
The formation of disulfide bonds via thiol-disulfide oxidoreductases (TDOR) is crucial for the proper folding and activity of many extracytoplasmic proteins. *Streptococcus gordonii* is a pioneer organism in the human oral cavity and a potential live oral vaccine vector. In this study we investigated the roles of two putative TDORs (Sgo1171 and Sgo1177) and their associated CcdA proteins in disulfide bond formation and the physiology of *S. gordonii.*

Methods:
Single and double mutants of the two TDORs and their *ccdA* genes were constructed via an allelic replacement strategy. Mutants were examined for the ability to produce a disulfide bonded-protein anti-CR1 single chain variable fragment (scFv) antibody by western blotting. Mutants were also analyzed for autolysis, extracellular DNA (eDNA) release, bacteriocin production, genetic competence, and oxidative stress.

Results:
Each of the *ccdA* and TDOR mutants, except for Δ*sgo1177*, was sensitive to 10 mM H_2O_2, indicating an important function in oxidative stress resistance. The Δ*ccdA2*, Δ*ccdA2/sgo1171*, Δ*ccdA2/sgo1177*, and Δ*sgo1171/sgo1177* mutants also produced dramatically lower amounts of the disulfide bonded protein anti-CR1 scFv, suggesting that these enzymes have multiple roles in the cell. Additional phenotypes were only observed in double mutants, consisting of different combinations of *ccdA* and TDOR genes. The Δ*ccdA2*/*sgo1171* and Δ*ccdA2*/*sgo1177* double mutants were resistant to autolysis and failed to release eDNA. Analysis of genetic competence revealed that Δ*ccdA2*/*sgo1171* double mutants showed a 1000-fold reduction in transformation frequency, while mutation of Δ*ccdA1*/*sgo1177*, or Δ*ccdA1*/*sgo1171* resulted in a 10-fold reduction in transformation frequency compared to the parent. Similarly, both Δ*ccdA2*/*sgo1171* and Δ*ccdA1*/*sgo1177* double mutants lacked bacteriocin activity.

Conclusions:
Taken together our results reveal that both TDORs (Sgo1171 and Sgo1177) and their associated CcdA proteins play a role in extracellular oxidative stress resistance in *S. gordonii*. However, CcdA2/Sgo1171, but not CcdA1/Sgo1177, showed an important role in disulfide bond formation. CcdA2/Sgo1171 affects multiple phenotypes in *S. gordonii*, whereas CcdA1/Sgo1177 appears to play a role in bacteriocin production and genetic competence.

17. KSHV MODULATES THE IRE1-XBP1 AXIS OF THE UNFOLDED PROTEIN RESPONSE DURING LYTIC REPLICATION

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(The author requested that this abstract not be published)

18. DEVELOPMENT OF A FRAMEWORK FOR CORRECTIONAL FACILITY BASED INTERVENTIONAL MEDICAL RESEARCH

AUTHORS: Oldford S[1], MacDonald K[2], Kempton K[2], Myers D[2], Barrett L[3,4]

AFFILIATION: [1]Department of Microbiology and Immunology, Dalhousie University; [2]Department of Environment, Labour, and Justice, Charlottetown, PEI. [3]Division of Infectious Disease, Department of Medicine, Dalhousie University, Halifax, NS [4]Capital District Health Authority, Halifax, NS

Introduction:
Incarcerated individuals have been excluded from interventional medical research for many years, however, there is increasing recognition that this may be discriminatory to individual detainees. There is no consensus on the best design to ensure ethical implementation of an interventional drug trial in an incarcerated population. We define a framework for ethical design and implementation of interventional research in an incarcerated population.

Methods:
A phase 4 study to treat hepatitis C virus (HCV) infection in an incarcerated population was used as a model. A literature review was performed to identify international experts in prison research, as well as identify existing best practices in prisoner health research. A broad range of community, academic, government and industry experts provided iterative feedback that was incorporated into study design.

Results:
The principles of equity (to research opportunities) and justice were recognized as key guiding ethical principles. A mechanism to assess informed consent and coercion were integral to ethical study implementation, and an independent study advisory board would be necessary to provide frequent review of participant feedback. Advisory board members must be separate from government custodians and the study team, reporting directly to the institutional study board. Additionally, all participants should have access to an independent advocate at all study visits if so desired. This framework was positively reviewed by a local research ethics board and given provisional approval.

Conclusions:
The framework developed through extensive consultation and literature review has been positively reviewed by an ethics board, and if successful in gaining final study approval, will provide ethical guidance for one of the first Phase 4 intervention studies in an incarcerated population in 60 years.

19. IMMUNOSENESCENCE AND FRAILTY IN A MURINE MODEL OF AGING

AUTHORS: Sharon Oldford[a,b], Susan Howlett[c,d] and Lisa Barrett[a,b,e]

AFFILIATION: [a]Senescence, Aging, Infection and Immunity Laboratory and Departments of [b]Microbiology and Immunology, [c]Pharmacology and Medicine (Divisions of [d]Geriatric Medicine and [e]Infectious Diseases)

Introduction:
Aged individuals exhibit decreased immunity characterized by clinical disease and functional changes in innate and adaptive immune responses. This immunologic aging is termed immunosenescence and is associated with increased rates of infection and poor immune responses to vaccination. Frailty is a state of increased susceptibility to adverse health outcomes and is increased in the elderly. Chronic inflammation is associated with a higher frailty index however the association between immunosenescence and frailty is presently unclear. Our objective is to determine if immunosenescence enhances frailty in the elderly by examining the relationship between immunosenescence and frailty in a murine model of aging.

Methods:
Frailty index is calculated in groups of young (5 month) and old (2+ years) adult mice using a non-invasive scoring system that measures deficits in 31 health-associated variables. Polychromatic flow cytometry is utilized to assess changes in the expression of immunosenescence cell surface markers on splenic natural killer, T cell, B cell and myeloid immune cell subsets. Quantitative changes in cell subset frequencies and proliferation are also assessed by flow cytometry. Immune parameters are compared to frailty index to determine if immunosenescence of innate (NK and myeloid cells) or adaptive (B cell and T cells) immune cell subsets associate with increased frailty in aging.

Results:
We will discuss preliminary flow cytometry data that outline a comprehensive strategy to characterize immunosenescence of innate and adaptive immune cell subsets in aging mice.

Conclusions:
These studies will provide novel insight into the relationships between aging, frailty and immunosenescence and may inform improved strategies to enhance immune function and vaccine responsiveness in the elderly.

20. URINARY PNEUMOCOCCAL ANTIGEN DETECTION TESTS: COMPARING DIAGNOSTIC PERFORMANCE IN ADULT COMMUNITY ACQUIRED PNEUMONIA (CAP) AND INVASIVE PNEUMOCOCCAL DISEASE (IPD)

AUTHORS: M. ElSherif[1], L Ye[1], D MacKinnon-Cameron[1], A Ambrose[1], T. Hatchette[1,3], J. Leblanc[1,3], and S. McNeil[1,2]on behalf of the Public Health Agency of Canada/Canadian Institutes of Health Research Influenza Research Network (PCIRN) Serious Outcomes Surveillance Network

AFFILIATION: [1]Canadian Center for Vaccinology, IWK Health Centre and Capital Health, Dalhousie University, [2]Division of Infectious Diseases, [3]Department of Medicine, Capital Health, [3]Department of Pathology and Laboratory Medicine, Capital Health

Introduction:
Definitive diagnosis of pneumococcal CAP and IPD is provisional to laboratory-confirmed detection of *S. pneumoniae*. In many systemic infections, bacterial antigens are excreted in urine rendering it a reservoir for potential diagnosis of infection. In our study, we compare the capacity of two urinary pneumococcal antigen detection tests in aiding the diagnosis of community acquired pneumonia (CAP) and invasive pneumococcal disease (IPD) presentations of pneumococcal infection among adults.

Methods:
The Public Health Agency of Canada/Canadian Institutes of Health Research (PCIRN) Serious Outcomes Surveillance (SOS) Network sponsors active surveillance for CAP and IPD in hospitalised Canadian adults. Patients who met inclusion criteria also provided a urine sample in addition to standard of care procedures to evaluate urinary antigen tests. The multiplex Luminex bead-based PCV13-serotype specific urine antigen detection (UAD) assay (developed by Pfizer) and the Binax NOW *Streptococcus pneumoniae* urinary antigen (BINAX) test (Alere International, Ireland) were assessed against the same sample set.

Results:
Among CAP and IPD cases enrolled from Dec 2010 to Dec 2012, 190 were positive by at least one of the following *S. pneumoniae* tests: culture, UAD and/or BINAX. Total *S. pneumoniae* positivity by “any test” was then used to assess the individual accuracy of UAD and BINAX. The UAD assay detected 142 of the 190 (74.74%), while the BINAX was positive in 96 (50.53%), with an associated p-value of <0.0001. For subjects that provided a urine sample paired with a clinical sample suitable for culturing, further analysis was done evaluating the performance of the UAD and BINAX against culture positives; the sensitivity and specificity of UAD and BINAX were 63.83% and 68.00 and 84.94 and 91.52, respectively.

Conclusions:
In our study, the UAD assay showed a significant diagnostic advantage over BINAX in the detection of pneumococcal CAP and IPD caused by PCV13 serotypes. Urine antigen detection tests are promising alternatives to culture-based diagnosis of pneumococcal pneumonia in certain settings and can be additionally advantageous through providing serotype data. While universal detection of the C-polysaccharide antigen present in all *S. pneumoniae* by the BINAX test provides increased sensitivity and specificity for the detection of *S. pneumonia* serotypes, the UAD has the added advantage of being able to distinguish serotypes covered by PCV13. With the poor sensitivity of both antigen detection methods, neither should be used as a standalone test for diagnosis of CAP and IPD, but these can provide value for pneumococcal surveillance.

21. RHAMNOSE BIOSYNTHESIS INHIBITORS AS POTENTIAL NEW ANTIBIOTICS

AUTHORS: David L. Jakeman, Nicole McCormick, Jian-She Zhu

AFFILIATION: Dalhousie University

Introduction:
New antibiotics are needed due to the development of bacterial resistance to those currently used clinically. We hypothesize that inhibitors of the L-rhamnose biosynthetic pathway may function as antibacterials due to the lack of this pathway in man and the requirement of the pathway for bacterial pathogenicity.

Methods:
Using chemical and enzymatic synthesis we completed the synthesis of a series of potential inhibitors. NMR spectroscopy was used to measure binding affinity of the inhibitors to rhamnose biosynthesis enzymes.

Results:
Using NMR spectroscopy we demonstrated that a number of these analogues are able to bind to the multiple enzymes in the pathway.

Conclusions:
We demonstrate the capacity for chemoenzymatic synthesis to deliver novel small molecules that function as inhibitors of the L-rhamnose biosynthetic pathway. Further studies are required to develop inhibitors into potential antibacterial compounds.

22. INTERIM ESTIMATES OF 2014/15 INFLUENZA VACCINE EFFECTIVENESS IN PREVENTING LABORATORY-CONFIRMED INFLUENZA-RELATED HOSPITALIZATION FROM THE SERIOUS OUTCOMES SURVEILLANCE (SOS) NETWORK OF THE CANADIAN IMMUNIZATION RESEARCH NETWORK (CIRN)

AUTHORS: S McNeil, M Andrew, T Hatchette, J Leblanc, M ElSherif, and L Ye on behalf of the Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS) Network Investigators

Introduction:
The 2014/15 influenza season in Canada has been characterized to date by early and intense activity dominated by influenza A(H3N2). Early antigenic and genetic characterization of circulating viruses suggest poor match with the influenza A(H3N2) component of the 2014/15 seasonal vaccine raising concern that vaccine effectiveness (VE) may be suboptimal. We provide interim estimates of influenza VE for the prevention influenza-related hospitalization amongst Canadian adults in order to inform public health communication and clinical decision-making mid-influenza season.

Methods:
In 2014/15 the SOS Network is conducting active surveillance for influenza among hospitalized adults beginning 15Nov2014 in 16 acute care facilities in 5 Provinces. A nasopharyngeal swab for influenza PCR was obtained from all adult patients admitted with an acute respiratory illness (community-acquired pneumonia, exacerbation of COPD/asthma, unexplained sepsis or any respiratory diagnosis or influenza-like symptom). Patients with a positive test for influenza are cases, while those testing negative for influenza within seven days of symptom onset are controls. VE was estimated as (1-OR) X 100 and adjusted for age and the presence of comorbidities.

Results:
600 cases and 471 test-negative controls were included in the interim analysis. Overall, 99.0% (593/599) of hospitalisations for laboratory-confirmed influenza were due to influenza A; influenza A (H3N2) accounted for 99.1% (n=214) of 216 cases with known subtype. Hospitalized patients with influenza were older than test-negative controls (mean age: 77.7y vs 70.9y, respectively; $p < 0.001$); 68.8% (n=413) of cases were over 75 years of age. The majority of cases and controls were female (54.2% and 52.7%, respectively; $p = 0.62$) and had one or more underlying medical comorbidity (97.2% and 97.0%, respectively; $p = 0.85$). 66.5% of cases and 63.7% of controls reported receipt of the 2014/15 influenza vaccine. Rates of admission to an intensive-care unit (10.1% vs 11.1%; $p = 0.64$), need for mechanical ventilation (4.2% vs 4.6%; $p = 0.85$), and death (7.9% vs 9.7%; $p = 0.46$) did not differ between cases and controls. Interim unmatched VE adjusted for age and presence of one or more comorbidities were −16.8% (90%CI: −48.9 to 8.3) overall and −22.0% (90% CI: −66.5 to 10.7) for laboratory-confirmed influenza A(H3N2). Among adults aged under 65 years, the overall VE was 10.8% (90% CI: −50.2 to 47.0) while in adults aged 65 years or older, the overall VE was −25.4% (90% CI: −65.0 to 4.6).

23. EFFICACY AND IMMUNOGENICITY OF A NOVEL 9-VALENT HPV L1 VIRUS-LIKE PARTICLE VACCINE IN 16-26 YEAR OLD WOMEN

AUTHORS: McNeil SA, Langley JM, Halperin SA on behalf of the V503 Study Team

Introduction:
Quadrivalent HPV (qHPV) vaccine is highly effective against HPV types 6 and 11, the cause of ~90% of external genital warts and HPV 16 and 18, the cause of ~70% of cervical cancer and a significant contributor to other cancers in males and females. While qHPV offers some cross-protection against non-vaccine HPV types, this protection is incomplete and short-lived. To optimize cancer prevention, an investigational 9-valent (6/11/16/18/31/33/45/52/58) HPV (9vHPV) vaccine which includes the 4 HPV types (6/11/16/18) in qHPV vaccine and the next 5 most common cancer-causing types (31/33/45/52/58) has been developed. Here we assess immunogenicity of 9vHPV vaccine in women 16-26y to demonstrate immunological non-inferiority of the HPV 6/11/16/18 response and efficacy of 9vHPV against HPV 31/33/4/52/58-related persistent infection and disease.

Methods:
14,204 healthy 16-26 year-old women were enrolled into an international, double-blind efficacy and immunogenicity study of the 9vHPV vaccine (controlled with qHPV). Subjects received 9vHPV vaccine or qHPV as a series of injections at day 1, month 2 and month 6. Primary Immunogenicity and efficacy analyses included subjects who were seronegative at day 1 and PCR negative from day 1 through month 7 for the HPV type being analyzed. Gynecological swabs (for HPV DNA testing) and Pap test were performed every 6 months. Subjects with abnormal Pap tests were referred to colposcopy using a protocol-mandated triage algorithm. Tissue obtained via biopsy/definitive therapy was tested for HPV types 6/11/1/6/18/31/33/35/39/45/51/52/56/58/59. Endpoints were adjudicated by a pathology panel.

Results:
Anti-HPV 6/11/16/18 responses generated by 9vHPV vaccine were non-inferior to those generated by qHPV vaccine. Efficacy of 9vHPV vaccine against a composite endpoint of HPV 31/33/45/52/58-related high-grade cervical/vulvar/vaginal disease was 96.7% ([95% CI: 80.9-99.8] 1 case in the 9vHPV vaccine group and 30 cases in the qHPV vaccine group). Efficacy against HPV 31/33/45/52/58-related cervical/vulvar/vaginal disease (any grade) in the PPE was 97.1% (95% CI: 91.8, 99.2). Efficacy against HPV 31/33/45/52/58-related 6-month persistent infection in the PPE was 96.0% (95% CI: 94.4-97.2).

Conclusions:
The 9vHPV vaccine was highly efficacious in preventing HPV 31/33/45/52/58-related persistent infection and disease. HPV6/11/16/18 immune responses were non-inferior to qHPV vaccine. Use of 9vHPV could prevent up to 90% of cervical cancer.

24. PHARMACISTS AS IMMUNIZERS: A SURVEY OF NEW BRUNSWICK PHARMACISTS' EXPERIENCES

AUTHORS: J. Isenor[1,2], K. Slayter[1,2], S. McNeil[1], D. MacDougall[1,4], S. Bowles[1,2,3]

AFFILIATION: [1] Canadian Center for Vaccinology, IWK Health Centre and Capital Health, Dalhousie University, [2] College of Pharmacy, Dalhousie University, [3] Department of Pharmacy, Capital Health, [4] School of Nursing, St. Francis Xavier University

Introduction:
There are limited data evaluating the experiences of Canadian pharmacists in their novel role as immunizers and no published data on the experiences of Maritime pharmacists who immunize.

Methods:
An anonymous, self-administered, web-based survey was offered via email by the New Brunswick Pharmacists' Association to all of its members. The survey tool was adapted, with permission, from a tool previously used by the American Pharmacists Association, and validated using content validity and test-retest reproducibility.

Results:
The survey response rate was 28% (180/635); however, survey responses were incomplete for 58 respondents. Approximately 90% of respondents worked in community practice full time, 65% were female and 44% were practicing for 20 or more years. The majority (86%) reported having received all required adult immunizations and 93% reported receipt of the annual influenza vaccine. The majority of patients immunized by pharmacists were adults 18 years of age and older. Greater than 75% reported administering: hepatitis A and B, influenza, and varicella- zoster. Of the estimated 15,000 vaccines administered by respondents, seven adverse events were reported, 6 were vasovagal and 1 was suspected anaphylaxis. The majority of respondents felt fully accepted as immunization providers by patients, with about 97% reporting agreement or strong agreement. Seventy percent or more agreed or strongly agreed that they had been fully accepted as an immunization provider by local physicians and health departments. Respondents reported immunization referrals from physicians, nurses, and public health (85%, 43% and 32%, respectively). Most commonly reported barriers were: lack of a universally funded influenza immunization program in NB, insufficient staffing, and concerns around reimbursement for services.

Conclusions:
NB pharmacists are actively participating in the provision of a variety of immunizations, with support from patients and other health care professionals.

25. INFLUENZA RISK FACTORS, OUTCOMES, AND VACCINE EFFECTIVENESS AMONGST ADULT PATIENTS WITH CHRONIC KIDNEY DISEASE ADMITTED WITH ACUTE RESPIRATORY ILLNESS (ARI); 2010/11 TO 2013/14: A CIRN SERIOUS OUTCOMES SURVEILLANCE (SOS) NETWORK STUDY

AUTHORS: G Wilson, S McNeil, M Andrew, L Ye and **K Tennankore**

AFFILIATION: The Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS) Network Investigators & Departments of Nephrology, Infectious Diseases, Geriatrics

Introduction:
Patients with chronic kidney disease (CKD) are at increased risk of influenza complications and vaccination may be less effective in this population. We sought to characterize risk factors and outcomes of influenza among hospitalized adults with CKD and to assess the effectiveness (VE) of seasonal influenza vaccines in the prevention of hospitalization in this high-risk group.

Methods:
From 2010/11 - 2013/14, the CIRN SOS Network conducted active surveillance for influenza among hospitalized adults from ~15Oct to 30April each season in up to 45 hospitals in 7 Provinces. A nasopharyngeal swab for influenza RT-PCR was obtained from patients admitted with acute respiratory illness. Patients were considered to have chronic renal disease if they were on chronic dialysis or if they had a baseline serum creatinine greater than 200 mmol/L. Cases were hospitalized IC adults testing positive for influenza; controls were influenza-negative. Immunization status was verified with the provider where possible. Vaccine effectiveness (VE) estimates were adjusted using multivariable conditional logistic regression. VE was estimated as (1-OR) X 100.

Results:
From 2010-2014, 410 patients with CKD were enrolled. CKD patients with lab-confirmed influenza (n=197) were younger than controls (70.2y vs 73.6y; p= 0.02) and were less likely to be past or current smokers (45.7% vs 54.9%; p=0.002). 62% of patients with CKD had received seasonal influenza vaccine. Among CKD patients with influenza, 50 (25.4%) required ICU admission, 31 (15.7%) were ventilated and 24 (12.2%) died. Overall, VE in CKD patients was 50% (90% CI: 27% -66%) adjusted for age, smoking and number of medications. Amongst the subset of CKD patients on dialysis (n=162), adjusted VE was 67% (90% CI: 39%-82%).

Conclusions:
Influenza is associated with considerable morbidity, mortality and healthcare utilization in adults with CKD. Influenza vaccine offers considerable protection with 50% effectiveness in the prevention of hospitalization but is underutilized; only 62% of hospitalized patients with CKD were vaccinated. VE remains quite high even in patients on dialysis where VE of 67% was observed. Efforts are needed to improve coverage in this vulnerable population.

26. CORRELATION OF THE BIOPLEX TEST AND PLAQUE REDUCTION NEUTRALIZATION TEST (PRNT) FOR DETERMINING IMMUNITY TO MEASLES VIRUS

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Introduction:
Seroepidemiology can be used to parameterize mathematical models for predicting risk for measles outbreaks if validated tests of immunity are available. The objectives of this study are: 1) To validate that the BioPlex can generate quantitative values. 2) To validate the quantitative BioPlex method against PRNT, the reference method for determining measles immunity

Methods:
To generate a calibration curve, two-fold serial dilutions of the WHO standard were tested on the BioPlex in triplicate. The Relative Fluorescence Intensity from the BioPlex were used to generate a calibration curve to allow the calculation of titres (in mIU/mL). Further validation included the testing of 148 patient specimens by the BioPlex and PRNT. Numeric titres and qualitative categorical results of the BioPlex assay were compared to the PRNT results.

Results:
The WHO standard the calibration curve allowed RFI to be translated into mIU/ml with total precision between 15 and 20%. BioPlex and PRNT results exhibited a reasonable correlation following an exponential function. The correlation is better for “non-equivocal” immune specimens,with poor correlation in specimens with low titre. Using a Receiver Operating Characteristics (ROC) analysis we established an equivocal zone for the BioPlex between ≥5mIU/ml and <70 mIU/mL that would require retesting with PRNT to ensure accurate determination of immunity.

Conclusions:
The BioPlex can generate quantitative measles titres. However, low titres require confirmation using PRNT. By determining an equivocal range requiring confirmation by PRNT, we can ensure accurate results for seroepidemiological studies.

27. DETECTION OF ENTEROVIRUS D68 IN CANADIAN LABORATORIES

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Introduction:
In late summer and early fall of 2014, widespread enterovirus type D68 (EV-D68) activity was described across North America with severe cases described in the US. In some cases, EV-D68 was associated with acute flaccid paralysis, and fatal cases have been documented. While nucleic acid amplification tests (NAATs) have become the method of choice for the detection of respiratory viruses like enteroviruses, there is evidence that detection methods vary in their performance characteristics, including analytical sensitivity. This study compared the analytical sensitivity of laboratory-developed tests (LDT) and commercially available NAATs used in hospital-based and provincial public health laboratories across Canada for the detection of EV-D68.

Methods:
The lower limit of detection (LoD) of each method was determined by testing 10-fold serial dilutions of RNA extracted from cultured EV-D68. Five replicates of each RNA dilution was shipped to participating sites. The estimated LoD for each assay was defined by Probit analysis using a probability of 95% and values were expressed as number of target copies/ml.

Results:
Our data demonstrated considerable variability in performance characteristics of assays used to detect EVD68 across Canada. Of particular interest, the Seegene RV15 and RV16 assays failed to detect EV-D68.

Conclusions:
Coordinated surveillance and detection algorithms are key in the understanding of the scope of spread and spectrum of EV-D68 disease. As with any emerging pathogen, it is important to understand the limitations of each molecular assay for the detection of EV-D68 and the comparability of assays offered by reference testing services. This study provides the first report comparing the analytical sensitivity of LDTs and commercial NAATs used in Canadian laboratories for the detection of EV-D68.

28. A VITAL CONTROL OF INTRACELLULAR *CHLAMYDIA* INFECTION REQUIRES INTERLEUKIN-17 RECEPTOR-MEDIATED SIGNALING

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Introduction:
IL-17A is a pleiotropic proinflammatory cytokine that has a vital role in host resistance against extracellular bacterial and fungal infections. However, its role in controlling intracellular bacterial infections remains elusive. Here, we examined the IL-17/IL-17 receptor-mediated signaling in controlling intracellular *Chlamydia muridarum* (*Cm*) infection in non-hematopoietic cells *in vitro* and *in vivo*.

Methods:
To examine whether the non-hematopoietic structural cells play an important role in controlling *Chlamydia* replication through the IL-17/IL-17R signaling *in vitro*, mouse embryonic fibroblast cells (MEFs) from wild-type (WT), IL-17RA-knockout (IL-17RAKO), and IL-17RC-knockout (IL-17RCKO) mice were infected with *Cm.* Changes in the intracellular signalling pathway correlating to changes in the cytokine response and bacterial burden were examined. To follow up on this approach *in vivo*, a respiratory *Chlamydia* infection model was established in bone marrow (BM) chimeric mice using WT BM donor cells transferred into γ-irradiated WT, IL-17RAKO and IL-17RCKO mice.

Results:
Remarkably, *Chlamydia* replication in MEFs was significantly increased in IL-17RCKO MEF and, to a lesser extent, in IL-17RAKO MEF compared to WT MEF at 6 and 12 hours post-infection. Both IL-17RAKO and IL-17RCKO BM chimeric mice had significantly elevated bacterial burden in the lung compared to WT mice at days 5 and 11 post infection. However, IL-17RCKO, but not IL-17RAKO, BM chimeric mice exhibited significant body weight loss compared to WT mice during early infection. While IL-17RAKO BM chimeric mice displayed an increased IL-17A response, IL-17RCKO mice showed an increased IFN-γ response in the lung.

Conclusions:
Our data demonstrates an indispensable role of the IL-17RC-mediated signaling in controlling *Chlamydia* infection and suggests differential roles of IL-17RA- and IL-17RC-mediated signaling in shaping *Chlamydia*-induced host responses.

29. IMPACT OF PHARMACISTS AS IMMUNIZERS ON INFLUENZA VACCINATION IN NOVA SCOTIA

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Introduction:
Immunization coverage in Canada remains below national goals with significant patient barriers to immunization, such as accessibility, being reported. Pharmacists are among the most accessed health-care providers and play an important role as vaccine educators, advocates, and more recently as administrators of immunizations. The benefits of the addition of pharmacists as vaccine administrators have been well documented in the U.S., however there are limited data on the impact of pharmacists as immunizers in Canada, and no published data exists on the impact of pharmacists as immunizers in Nova Scotia (NS).

Methods:
Influenza vaccination coverage rates in NS were determined by analyzing the number of vaccines administered by primary care providers, public health, and pharmacists as a proportion of the census data from the respective year. The coverage rates in the first influenza season in which pharmacists were regulated to administer publicly funded influenza immunizations (2013/14) were compared to coverage in the previous influenza seasons post-pH1N1 in which there was a universal influenza program (2010/11 to 2012/13). Influenza vaccination was also compared by age group and gender to determine if immunization rates have changed in a specific demographic.

Results:
In the year that pharmacists began administering immunizations in NS (2013/14), influenza vaccination rates for those 5 years of age and older increased to 41.6%, a 5.9% increase from the previous year (2012/13). There was a cumulative 2.8% decline in vaccination provision by physicians and public health in 2013/14. Pharmacists administered just over 78,000 influenza vaccinations, accounting for nearly 9% of the NS population over the age of 5. Influenza vaccine coverage rates for those 65 and older increased by 9.8% in the year pharmacists began immunizing, with pharmacists vaccinating 13.5% of this population.

Conclusions:
Influenza vaccination coverage in NS increased in the first year that pharmacists provided influenza vaccines compared to previous years with a universal influenza program. Various factors may have contributed to the increased coverage, including the addition of pharmacists as immunizers, as well as media coverage of influenza related fatalities. Future research will be necessary to fully determine the impact of pharmacists as immunizers and other factors on immunization rates.

30. FUSOGENIC REOVIRUSES GENERATE INFECTIOUS VESICLE-ENCAPSULATED NONENVELOPED VIRUS (VENEV) PARTICLES AND FUSOGENIC EXOSOMES

AUTHORS: Chungen Pan[1], Jolene Read[1], Roberto de Antueno[1], Elizabeth Castle[1] and Roy Duncan[1,2,3*]

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Introduction:
Almost all viruses encode at least one small membrane-associated protein, collectively referred to as viroporins (e.g. HIV vpu, influenza virus M2, hepatitis C virus p7, poliovirus 2B). This subclass of viral proteins are adept at remodelling cell membranes and reprogramming membrane biogenesis pathways to promote virus replication, assembly and release. The reovirus fusion-associated small transmembrane (FAST) proteins are a unique subgroup of viroporins that induce cell-cell fusion and syncytium formation, promoting virus dissemination and pathogenesis.

Methods:
A yeast two-hybrid screen identified components of the exosome pathway as genetic interaction partners of the FAST proteins. OptiPrep gradients, immunoblotting, biochemical assays, inhibitor studies and electron microscopy were performed to confirm these interactions and establish their significance.

Results:
We discovered that FAST proteins upregulate exosome biogenesis and the release of fusogenic FAST protein-containing exosomes. Results indicate the p14 FAST protein interacts with components of the ESCRT machinery and Rab-dependent vesicular trafficking pathways. Inhibitor studies revealed that both of these pathways are involved in the generation of FAST protein-exosomes, and are also somehow connected to FAST protein-mediated syncytiogenesis. Most interestingly, reovirus particles are released as infectious vesicle-encapsulated nonenveloped virus (VENEV) particles inside exosomes.

Conclusions:
These results indicate exosome biogenesis and cell-cell fusion pathways are interconnected, and that FAST proteins promote reovirus dissemination and pathogenesis by inducing formation of both syncytia and infectious VENEVs.

31. REFINING PCR-BASED SURVEILLANCE OF VACCINE-PREVENTABLE SEROTYPES OF STREPTOCOCCUS PNEUMONIAE

AUTHORS: J. LeBlanc[1], A.L.S. Lang[1], M. El-Sherif[1], I. Martin[2], T.F. Hatchette[1], and S. McNeil[1] and on behalf of the Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS) Network Investigators

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Introduction:
To monitor the serotype distribution of *S. pneumonia* and assess the impact of pneumococcal vaccines, PCR-based serotyping assays have been developed. Given that these methods can require up to 8 conventional multiplex PCR (cmPCR) or 7 real-time multiplex PCR (rmPCR) reactions to assign a serotype, testing is often conducted as sequential algorithm. This study used a modified set of cmPCR and rmPCR reactions (termed cmPCRmod and rmPCRmod) to focus on the identification of serotypes covered by the 7- and 13-valent pneumococcal conjugate vaccines, and the 23-valent pneumococcal polysaccharide vaccine (PCV7, PCV13, and PPV23, respectively).

Methods:
308 *S. pneumoniae* isolates characterized by Quellung serotyping were subjected to PCR-based serotype deduction using cmPCR, cmPCRmod, rmPCR, and rmPCRmod. Analytical sensitivity for each molecular method was evaluated using serial 10-fold dilutions of representative *S. pneumoniae* serotypes for each reaction, and analytical specificity was compared with a panel of non-pneumococcal isolates and pre-characterized *S. pneumoniae* serotypes.

Results:
Equivalent analytical sensitivity and specificity was seen when comparing cmPCR and cmPCRmod or rmPCR and rmPCRmod, and 100% concordance between these methods was observed with 308 clinical isolates of *S. pneumoniae*. However, compared to cmPCR, cmPCRmod reduced the number of reactions required to detect serotypes covered by PCV7, PCV13, and PPV23 by 44%, 33%, and 8%, respectively. Similarly rmPCRmod required 54% and 22% less reactions to identify vaccine-serotypes covered by PCV7 and PCV13, respectively.

Conclusions:
Overall, this study demonstrated that conventional and real-time multiplex reactions can be reformulated for more efficient detection of *S. pneumoniae* serotypes found in current pneumococcal vaccines, which could provide significant cost savings for large epidemiological studies.

32. REGULATION OF TRANSLATION IN KAPOSI'S SARCOMA

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(The author requested that this abstract not be published)

33. ADVERSE EVENT FOLLOWING IMMUNIZATION SURVEILLANCE SYSTEMS FOR PREGNANT WOMEN AND THEIR INFANTS: A SYSTEMATIC REVIEW

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Introduction:
The World Health Organization's Strategic Advisory Group of Experts on Immunization has declared that maternal immunization is a key priority. Robust adverse event following immunization (AEFI) surveillance systems that capture outcomes in pregnant women and their infants are needed to ensure the safety of maternal immunization programs. We sought to identify the active and passive AEFI surveillance systems for pregnant women and their offspring described in the literature.

Methods:
A systematic literature review was conducted of the MEDLINE, CINAHL, and EMBASE databases from 1990 to 2014 to identify the active and passive AEFI surveillance systems for pregnant women and their offspring that have been described. English-language articles were reviewed if they included pregnant women as the population of interest and described the surveillance method used

Results:
Of 619 articles retrieved from the search, 16 met the criteria for review. These included reports of AEFI surveillance for pregnant women, their offspring, or both. The majority of reports (11/16) came from the United States and described findings on two active and four passive AEFI surveillance systems, only three of which specifically targeted pregnant women. The remaining five articles described one-time AEFI surveillance programs, all in high-income countries.

Conclusions:
There are no published reports outside of the United States of ongoing AEFI surveillance systems that specifically target pregnant women or their offspring. There may be AEFI surveillance systems that capture events in these populations that have not been reported in the literature. A survey of Immunization Program Managers and National Regulatory Authorities is needed to determine the current status of AEFI surveillance for pregnant women and their offspring globally.

34. NOVEL *BORDETELLA PERTUSSIS* VACCINES FORMULATED USING THE DEPOVAX™ PLATFORM CONFER LONG-LASTING IMMUNITY IN MICE

AUTHORS: Sarah M. McAlpine[1,3,4], Ann MacMillan[3], Lisa D. MacDonald[5], Marianne M. Stanford[1,3,5], Marc Mansour[3,5], Song F. Lee[1,3] and Scott A. Halperin[1,2,3,4]

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Introduction:
Pertussis, or whooping cough, is a contagious infection of the upper and lower airways caused by the bacterium *Bordetella pertussis* (Bp). Pertussis results in morbidity and mortality, particularly in young children. While current vaccines protect against Bp, multiple doses are needed and immunity wanes by early adulthood. DepoVax™, can enhance antigen uptake and drive Th1 immunity, and is currently in clinical trials as a cancer vaccine. We aim to understand how DepoVax™ may protect from Bp.

Methods:
Mice were vaccinated i.m. with DepoVax™ vaccine containing genetically-detoxified Bp toxin, currently-licensed DTaP vaccine or saline. Mice were then challenged with aerosolized Bp and bacterial clearance from the lung was evaluated on days 7 and 15 post-infection. Cellular immunity was assessed by antigen restimulation of splenocytes followed by analysis of cytokine production by ELISA. Anti-Bp antibody titres in sera were also measured by ELISA.

Results:
Mice vaccinated with a single dose of DepoVax™-Bp cleared the infection as well as mice that received two doses of DTaP. ELISA showed that DepoVax™-Bp induced higher antibody titres than DTaP, particularly the IgG2a isotype. Long-term studies revealed that this immunity was maintained up to 5 months post-vaccination. Antigen restimulation of splenocytes from mice vaccinated with DepoVax™-Bp demonstrated strong IFN-γ production on day 28 with little IL-13 compared to splenocytes from mice vaccinated with DTaP. By day 170, IFN-γ production was elevated in mice vaccinated with DepoVax™-Bp, while IFN-γ production was not sustained in DTaP-vaccinated mice.

Conclusions:
Vaccines formulated with the DepoVax™ platform can induce improved immunity to Bp that results in sustained and balanced Th1 and Th2 immune responses in mouse models of lung infection. These preliminary findings may ultimately lead to the introduction of new pertussis vaccines that are longer lasting and require fewer doses.

35. PAIN MITIGATION DURING ADULT VACCINE INJECTIONS

AUTHORS: Kathryn Cull[1], Jennifer Isenor[2,3], Shelly McNeil[3,4], Mary Appleton[3], Noni MacDonald[3,5], Susan Bowles[2], Beth Halperin[3], Kathryn Slayter[1,2,3,4], Audrey Steenbeek[6], Anna Taddio[7,8], Lucie Bucci[9]

AFFILIATION: [1]Dalhousie University, School of Medicine, [2]Dalhousie University, College of Pharmacy, [3]Canadian Center for Vaccinology, [4]Dalhousie University Department of Medicine Division of Infectious Diseases, Capital Health, [5]IWK Health Centre, Halifax, Nova Scotia, [6] School of Nursing, Dalhousie University, [7]University of Toronto, [8]The Hospital for Sick Children, Toronto, Ontario, [9]Immunize Canada, Ottawa, Ontario,

Introduction:
Although there are many contributing factors for adults who decide against vaccination, data suggests that fear of pain from immunization is an important one. An evidence-based pamphlet to reduce immunization pain in children has previously been published in Canada; however, a similar pamphlet has not yet been developed for adults. Our objective was to develop a tool to support pain mitigation during adult immunizations.

Methods:
A systematic review of adult pain mitigation interventions was completed and compared to the pediatric evidence. A multidisciplinary team with expertise in vaccinology developed an evidence-based tool for pain mitigation during adult immunizations. The tool was focus-tested with three groups: health care professionals, health care professional students, and the general public. Participants provided feedback on the readability, usability, visual appeal and novelty of content of the tool.

Results:
The multi-disciplinary team systematically reviewed the literature and an evidence-based pamphlet for adult pain mitigation was developed. The pamphlet includes evidence-based recommendations on topical anesthetics, body position, and distraction. The pamphlet has been focus tested with three groups: health care professionals, health care professional students, and the general public. The preliminary results of the focus groups have been positive with only minor formatting suggestions.

Conclusions:
An adult pain mitigation pamphlet was developed and focus group tested. Future plans include further focus group and one-on-one testing followed by pilot testing of the tool in local hospitals. The tool will then be distributed and evaluated for impact in the community.

36. 4T1-MURINE MAMMARY CARCINOMA CELLS ENHANCE MACROPHAGE-MEDIATED INNATE-INFLAMMATORY RESPONSES.

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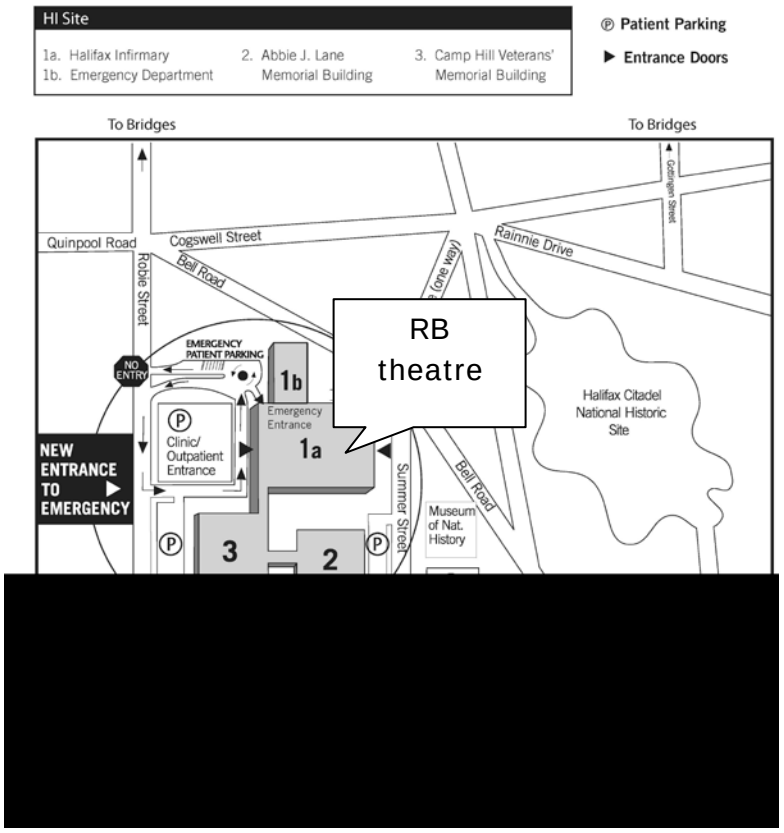
Introduction:
In cancer patients, the tumor has profound effects on the host immune response. While it is known that cancers alter the inflammatory response to their benefit, promoting tumor growth and dissemination, little is known regarding how cancers affect host defense against pathogens. In this study, we investigated the effects of tumors on the inflammatory responses of macrophages, a central population in host defense.

Methods:
Macrophages were conditioned with tumor secretions for 24 h prior to assessment of their inflammatory phenotype through stimulation with TLR agonists. This included the TLR-induced secretion of inflammatory cytokines, production of reactive oxygen and nitrogen species, and phagocytic behavior of tumor-conditioned macrophages.

Results:
4T1 mammary carcinoma-conditioned macrophages demonstrated enhanced production of pro-inflammatory cytokines TNFα and IL-6, but not IL-10, compared to control macrophages after stimulation with bacterial motifs LPS, peptidoglycan, and flagellin. In addition, 4T1-conditioned macrophages showed enhanced production of reactive nitrogen species in response to bacterial agonists and demonstrated enhanced phagocytosis of *E. coli* particles.

Conclusions:
Our investigations demonstrate that secretions from tumor cells can have significant effects on macrophage behavior. 4T1-conditioned macrophages exhibit heightened innate inflammatory responses when exposed to bacterial patterns. These findings have significant implications on the host defense responses of cancer patients.

QEII Halifax Infirmary Site



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