<table>
<thead>
<tr>
<th>Presenting Author / Auteur Présentateur</th>
<th>Abstract Title / Titre d’abrégré</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STREAM 1: BASIC SCIENCE / ŠÉANCE 1 : SCIENCE FONDAMENTALE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Al-Alwan, Laila</td>
<td>Growth-Related Oncogene (GRO)-α Inhibition of Airway Smooth Muscle Cell Migration Is Mediated by the Decoy Receptor ‘Duffy Antigen Receptor for Chemokines’ DARC</td>
<td>e63</td>
</tr>
<tr>
<td>Barrier, Marjorie</td>
<td>CT-Angiograms and Pulmonary Vascular Remodeling in Pulmonary Arterial Hypertension</td>
<td>e63</td>
</tr>
<tr>
<td>Chang, Ying</td>
<td>Genetic Deletion of IL-17 Ameliorates Inflammatory Response and Airway Remodeling in a Mouse Model of Chronic Severe Asthma</td>
<td>e63</td>
</tr>
<tr>
<td>Lamontagne, Maxime</td>
<td>Expression Quantitative Trait Loci (eQTL) Mapping of the Major Histocompatibility Complex in Human Lung</td>
<td>e64</td>
</tr>
<tr>
<td>Meloche, Jolyane</td>
<td>The Advanced Glycation Endproducts Receptor: Novel Therapeutic Target of Pulmonary Arterial Hypertension</td>
<td>e64</td>
</tr>
<tr>
<td>Morissette, Mathieu</td>
<td>Cigarette Smoke Exposure Leads to the Generation of Oxidized LDL that Initiates Inflammatory Processes and Impairs Host Defense</td>
<td>e64</td>
</tr>
<tr>
<td><strong>STREAM 2: CLINICAL, ASTHMA / ŠÉANCE 2 : RECHERCHE CLINIQUE, ASTHME</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bénédé, Jean-Christophe</td>
<td>The Quebec City Case-Control Asthma Cohort</td>
<td>e65</td>
</tr>
<tr>
<td>Dauncey, Lynette</td>
<td>Importance of Identifying Body Distress in Patients With Severe Asthma – A Case Series</td>
<td>e65</td>
</tr>
<tr>
<td>Kirychuk, Shelley</td>
<td>Lung Function Associated With Chronic Conditions Among Those With And Without Asthma or COPD</td>
<td>e65</td>
</tr>
<tr>
<td>Sayegh-Smith, Jennifer</td>
<td>Relationship Between Airway Hyperresponsiveness and Clinical Asthma in Morbidly Obese Patients</td>
<td>e66</td>
</tr>
<tr>
<td>To, Teresa</td>
<td>The Prevalence of Severe Asthma in Ontario, Canada from 2003 to 2009</td>
<td>e66</td>
</tr>
<tr>
<td><strong>STREAM 3: CLINICAL, COPD / ŠÉANCE 3 : RECHERCHE CLINIQUE, MPOC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Camp, Pat</td>
<td>The Prevalence of Chronic Obstructive Pulmonary Disease (COPD) in Individuals With Diabetes, Hypertension, Asthma or Mood/Anxiety Disorders: A Canadian Population Study</td>
<td>e66</td>
</tr>
<tr>
<td>Camp, Pat</td>
<td>Mobility and Physical Function in Hospitalized Patients With an Acute Exacerbation of COPD</td>
<td>e67</td>
</tr>
<tr>
<td>Chan-Thim, Emilie</td>
<td>Actigraphic Assessment of Sleep Parameters in COPD in Relation to Anxiety and Depression Symptoms</td>
<td>e67</td>
</tr>
<tr>
<td>Duff Cloutier, Julie</td>
<td>A Decade of Qualitative Research in Chronic Obstructive Pulmonary Disease (COPD): A Meta-Method Study</td>
<td>e67</td>
</tr>
<tr>
<td>Horvey, Karla</td>
<td>Changes in Exertional Dyspnea After Singing Intervention in Pulmonary Rehabilitation Attendees</td>
<td>e67</td>
</tr>
<tr>
<td>Janaadis-Ferreira, Tania</td>
<td>Measurement of Activities of Daily Living in COPD: A Systematic Review</td>
<td>e68</td>
</tr>
<tr>
<td>Janaadis-Ferreira, Tania</td>
<td>Prevalence and Profile of Patients With a Diagnosis of COPD Participating in Non-Pulmonary Rehabilitation Programs</td>
<td>e68</td>
</tr>
<tr>
<td>Joubert, Alexandre</td>
<td>Exploring the Perspective of Healthcare Professionals on the Initiation of Advance Care Planning Discussions With COPD Patients and Their Families</td>
<td>e68</td>
</tr>
<tr>
<td>Rizk, Amanda</td>
<td>Relationship between Acute Affective and Symptomatic Responses to Exercise Training and Compliance to Pulmonary Rehabilitation in Chronic Obstructive Pulmonary Disease</td>
<td>e69</td>
</tr>
<tr>
<td>To, Teresa</td>
<td>The Impact of Air Quality on Chronic Obstructive Pulmonary Disease (COPD) Morbidity: A Population-Based Study</td>
<td>e69</td>
</tr>
<tr>
<td><strong>STREAM 4: INNOVATION / ŠÉANCE 4 : INNOVATION</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alahmadi, Turki</td>
<td>Long Term Home Ventilation of Patients With Duchenne Muscular Dystrophy</td>
<td>e69</td>
</tr>
<tr>
<td>Guez, Manon</td>
<td>Negative Pressure Wound Therapy in the Management of Open Window Thoracostomy (Thoracic Window)</td>
<td>e70</td>
</tr>
<tr>
<td>Larsen, Tania</td>
<td>A Retrospective Study of Acute Rehabilitation of Patients Who Experience Prolonged Weaning from Mechanical Ventilation in a Canadian Critical Care Trauma Centre</td>
<td>e70</td>
</tr>
<tr>
<td>Madeley, Carole</td>
<td>breathe: The Development of a Canadian Asthma Self-Management Web Application</td>
<td>e71</td>
</tr>
<tr>
<td>Mesbah, Amanda</td>
<td>A Simple Model for Teaching Chest Tube Insertion</td>
<td>e71</td>
</tr>
</tbody>
</table>
Milot, Ariane
Breathing Retraining Program for Hyperventilation Syndrome

Zarins, Sherry
Supervised Regular Exercise as an Aid to Smoking Cessation: A Study of the Quit & Get Fit Program

Athron, Sandra
Emergency Department Asthma Care Pathway Initiative of the Ontario Lung Association

Desveaux, Laura
Community-Based Exercise Programs as a Strategy to Maintain Function in Chronic Disease: A Systematic Review

Doucet, Mariève
A Quebec Knowledge Translation Model in Respiratory Disease Surveillance

Harkness, Howard
Not All Antistatic Valved Holding Chambers Have Equivalent Performance: An Example of Why Each Valved Holding Chamber (VHC)-Inhaler Combination Should Be Considered Unique

Kitchlu, Abhijat
Clinical Outcomes Following Implementation of an Evidence-Based Order Set for Inpatient COPD Exacerbation Management

Olajos-Clow, Jennifer
Provincial Implementation of an Emergency Department Asthma Care Pathway: Lessons Learned in Knowledge Translation

Small, Sandra
Asbestos-Related Disease in Former Workers of the Asbestos Mine in Baie Verte, Newfoundland and Labrador

Small, Sandra
The Development of an Occupational Disease Registry of Former Workers of the Asbestos Mine in Baie Verte, Newfoundland and Labrador

Kam, Karen
Surgical Versus Non-Surgical Interventions to Relieve Upper Airway Obstruction in Children With Pierre Robin Sequence

Keilty, Krista
Studies of Sleep Disturbance in Family Caregivers of Technology Dependent Children

Li, Abby
RSV Hospitalization in Cystic Fibrosis in the Canadian Registry of Palivizumab (CARESS) Following Prophylaxis (2005-2012)

Li, Abby
RSV Hospitalization in Aboriginal Infants in the Canadian Registry of Synagis® (CARESS) Following Prophylaxis (2005-2012)

Sokoluk, Sarah
A Comparison of Quality of Life (QOL) Perceptions: Children With Asthma and Their Caregivers

Coats, Valérie
Body Composition Analysis for Patient With Lung Cancer Using Computed Tomography Image Analysis

Hercun, Julian
Risk Factors for Postoperative Recurrence of Primary Spontaneous Pneumothorax, With an Emphasis on Cannabis Consumption

Labbé, Catherine
Diagnostic Yield of Flexible Bronchoscopy Without Guidance (Aspiration, Brushing, Bronchoalveolar Lavage) for Peripheral Pulmonary Neoplasia

Wickerson, Lisa
Functional Outcomes Pre- and Early Post-Lung Transplantation

Bordeleau, Martine
Evaluation of Gastroesophageal Reflux in Winter Athletes With Exercise-Induced Cough

Malenfant, Simon
Abnormal Peripheral Muscle Oxygenation during Submaximal Exercise in Pulmonary Arterial Hypertension

Mura, Marco
Osteopontin Lung Expression is a Marker of Disease Severity in Pulmonary Arterial Hypertension

Porlier, Alexandra
Expression of miR-204 in Vastus Lateralis Muscles of Patients With COPD

Potus, François
Role of miR-126 in Exercise Intolerance Seen in Pulmonary Arterial Hypertension

Provencher, Steeve
PIM-1: A New Biomarker in Pulmonary Arterial Hypertension

Seaton, Claire
Two Cases of Pseudohypoaldosteronism Type 1 With Novel Genetic Mutations: Life-Threatening Neonatal Salt Wasting and Hyperkalaemia With a Positive Sweat Test and CF-Like Illness

Tacon, Claire
Trends in Canadian Respiratory Clinical Trials from 2001-2011

Thain, Katherine
The Canadian Respiratory Journal – One Year On and Still Improving!

Al-Alwan, Laila
Growth-Related Oncogene (GRO)-α Inhibition of Airway Smooth Muscle Cell Migration Is Mediated by the Decay Receptor “Duffy Antigen Receptor for Chemokines” DARC

Alahmadi, Turki
Long Term Home Ventilation of Patients With Duchenne Muscular Dystrophy

Athron, Sandra
Emergency Department Asthma Care Pathway Initiative of the Ontario Lung Association

Barrier, Marjorie
CT-Angiograms and Pulmonary Vascular Remodeling in Pulmonary Arterial Hypertension

Bénabéd, Jean-Christophe
The Quebec City Case-Control Asthma Cohort

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<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chan-Thim, Emilie</td>
<td>Actigraphic Assessment of Sleep Parameters in COPD in Relation to Anxiety and Depression Symptoms</td>
<td>e67</td>
</tr>
<tr>
<td>Chang, Yung</td>
<td>Genetic Deletion of IL-17 Ameliorates Inflammatory Response and Airway Remodeling in a Mouse Model of Chronic Severe Asthma</td>
<td>e63</td>
</tr>
<tr>
<td>Coats, Valérie</td>
<td>Body Composition Analysis for Patient With Lung Cancer Using Computed Tomography Image Analysis</td>
<td>e76</td>
</tr>
<tr>
<td>Dauncey, Lynette</td>
<td>Importance of Identifying Body Distress in Patients With Severe Asthma– A Case Series</td>
<td>e65</td>
</tr>
<tr>
<td>Desveaux, Laura</td>
<td>Community-Based Exercise Programs as a Strategy to Maintain Function in Chronic Disease: A Systematic Review</td>
<td>e72</td>
</tr>
<tr>
<td>Doucet, Mariève</td>
<td>A Quebec Knowledge Translation Model in Respiratory Disease Surveillance</td>
<td>e72</td>
</tr>
<tr>
<td>Duff Cloutier, Julie</td>
<td>A Decade of Qualitative Research in Chronic Obstructive Pulmonary Disease (COPD): A Meta-Method Study</td>
<td>e67</td>
</tr>
<tr>
<td>Guez, Manon</td>
<td>Negative Pressure Wound Therapy in the Management of Open Window Thoracostomy (Thoracic Window)</td>
<td>e70</td>
</tr>
<tr>
<td>Harkness, Howard</td>
<td>Not All Antistatic Valved Holding Chambers Have Equivalent Performance: An Example of Why Each Valved Holding Chamber (VHC)-Inhaler Combination Should Be Considered Unique</td>
<td>e73</td>
</tr>
<tr>
<td>Hercun, Julian</td>
<td>Risk Factors for Postoperative Recurrence of Primary Spontaneous Pneumothorax, With an Emphasis on Cannabis Consumption</td>
<td>e76</td>
</tr>
<tr>
<td>Horvey, Karla</td>
<td>Changes in Exertional Dyspnea After Singing Intervention in Pulmonary Rehabilitation Attendees</td>
<td>e67</td>
</tr>
<tr>
<td>Janadas-Ferreira, Tania</td>
<td>Measurement of Activities of Daily Living in COPD: A Systematic Review</td>
<td>e68</td>
</tr>
<tr>
<td>Janadas-Ferreira, Tania</td>
<td>Prevalence and Profile of Patients With a Diagnosis of COPD Participating in Non-Pulmonary Rehabilitation Programs</td>
<td>e68</td>
</tr>
<tr>
<td>Joubert, Alexandre</td>
<td>Exploring the Perspective of Healthcare Professionals on the Initiation of Advance Care Planning Discussions With COPD Patients and Their Families</td>
<td>e68</td>
</tr>
<tr>
<td>Kam, Karen</td>
<td>Surgical Versus Non-Surgical Interventions to Relieve Upper Airway Obstruction in Children With Pierre Robin Sequence</td>
<td>e74</td>
</tr>
<tr>
<td>Keilty, Krisa</td>
<td>Studies of Sleep Disturbance in Family Caregivers of Technology Dependent Children</td>
<td>e75</td>
</tr>
<tr>
<td>Kirychuk, Shelley</td>
<td>Lung Function Associated With Chronic Conditions among Those With and Without Asthma or COPD</td>
<td>e65</td>
</tr>
<tr>
<td>Kitchlu, Abhujat</td>
<td>Clinical Outcomes Following Implementation of an Evidence-Based Order Set for Inpatient COPD Exacerbation Management</td>
<td>e73</td>
</tr>
<tr>
<td>Labbé, Catherine</td>
<td>Diagnostic Yield of Flexible Bronchoscopy Without Guidance (Aspiration, Brushing, Bronchoalveolar Lavage) for Peripheral Pulmonary Neoplasia</td>
<td>e77</td>
</tr>
<tr>
<td>Lamontagne, Maxime</td>
<td>Expression Quantitative Trait Loci (eQTL) Mapping of the Major Histo compatibility Complex in Human Lung</td>
<td>e64</td>
</tr>
<tr>
<td>Larsen, Tania</td>
<td>A Retrospective Study of Acute Rehabilitation of Patients Who Experience Prolonged Weaning from Mechanical Ventilation in a Canadian Critical Care Trauma Centre</td>
<td>e70</td>
</tr>
<tr>
<td>Li, Abby</td>
<td>RSV Hospitalization in Aboriginal Infants in the Canadian Registry of Synagis® (CARESS) Following Prophylaxis (2005-2012)</td>
<td>e75</td>
</tr>
<tr>
<td>Li, Abby</td>
<td>RSV Hospitalization in Cystic Fibrosis in the Canadian Registry of Pulaviumab (CARESS) Following Prophylaxis (2005-2012)</td>
<td>e75</td>
</tr>
<tr>
<td>Madeley, Carole</td>
<td>breathe: The Development of a Canadian Asthma Self-Management Web Application</td>
<td>e71</td>
</tr>
<tr>
<td>Malenfant, Simon</td>
<td>Abnormal Peripheral Muscle Oxygenation during Submaximal Exercise in Pulmonary Arterial Hypertension</td>
<td>e77</td>
</tr>
<tr>
<td>Meloche, Jolyane</td>
<td>The Advanced Glycation Endproducts Receptor: Novel Therapeutic Target of Pulmonary Arterial Hypertension</td>
<td>e71</td>
</tr>
<tr>
<td>Mesbah, Amanda</td>
<td>A Simple Model for Teaching Chest Tube Insertion</td>
<td>e71</td>
</tr>
<tr>
<td>Milot, Ariane</td>
<td>Breathing Retraining Program for Hyperventilation Syndrome</td>
<td>e71</td>
</tr>
<tr>
<td>Morissette, Mathieu</td>
<td>Cigarette Smoke Exposure Leads to the Generation of Oxidized LDL that Initiates Inflammatory Processes and Impairs Host Defense</td>
<td>e64</td>
</tr>
<tr>
<td>Mura, Marco</td>
<td>Osteopontin Lung Expression is a Marker of Disease Severity in Pulmonary Arterial Hypertension</td>
<td>e78</td>
</tr>
<tr>
<td>Olajos-Clow, Jennifer</td>
<td>Provincial Implementation of an Emergency Department Asthma Care Pathway: Lessons Learned in Knowledge Translation</td>
<td>e73</td>
</tr>
<tr>
<td>Pohler, Alexandra</td>
<td>Expression of miR-204 in Vastus Lateralis Muscles of Patients With COPD</td>
<td>e78</td>
</tr>
<tr>
<td>Potus, François</td>
<td>Role for miR-126 in Exercise Intolerance Seen in Pulmonary Arterial Hypertension</td>
<td>e78</td>
</tr>
<tr>
<td>Provencer, Steeve</td>
<td>PIM-1: A New Biomarker in Pulmonary Arterial Hypertension</td>
<td>e79</td>
</tr>
<tr>
<td>Riek, Amanda</td>
<td>Relationship between Acute Affective and Symptomatic Responses to Exercise Training and Compliance to Pulmonary Rehabilitation in Chronic Obstructive Pulmonary Disease</td>
<td>e69</td>
</tr>
<tr>
<td>Sayegh-Smith, Jennifer</td>
<td>Relationship between Airway Hyperresponsiveness and Clinical Asthma in Morbidly Obese Patients</td>
<td>e66</td>
</tr>
<tr>
<td>Seaton, Claire</td>
<td>Two Cases of Pseudohypoaldosteronism Type 1 With Novel Genetic Mutations: Life-Threatening Neonatal Salt Wasting and Hyperkalaemia With a Positive Sweat Test and CF-Like Illness</td>
<td>e79</td>
</tr>
<tr>
<td>Small, Sandra</td>
<td>Asbestos-Related Disease in Former Workers of the Asbestos Mine in Baie Verte, Newfoundland and Labrador</td>
<td>e74</td>
</tr>
<tr>
<td>Small, Sandra</td>
<td>The Development of an Occupational Disease Registry of Former Workers of the Asbestos Mine in Baie Verte, Newfoundland and Labrador</td>
<td>e74</td>
</tr>
<tr>
<td>Sokoluk, Sarah</td>
<td>A Comparison of Quality of Life (QOL) Perceptions: Children With Asthma and Their Caregivers</td>
<td>e76</td>
</tr>
<tr>
<td>Tacon, Claire</td>
<td>Trends in Canadian Respiratory Clinical Trials from 2001-2011</td>
<td>e79</td>
</tr>
<tr>
<td>Thain, Katherine</td>
<td>The Canadian Respiratory Journal – One Year On and Still Improving!</td>
<td>e80</td>
</tr>
<tr>
<td>Thériault, Marie-Eve</td>
<td>Peripheral Skeletal Muscle: Characterization of Its Regenerative Potential in Patients With Chronic Obstructive Pulmonary Disease</td>
<td>e80</td>
</tr>
<tr>
<td>To, Teresa</td>
<td>The Impact of Air Quality on Chronic Obstructive Pulmonary Disease (COPD) Morbidity: A Population-Based Study</td>
<td>e69</td>
</tr>
<tr>
<td>To, Teresa</td>
<td>The Prevalence of Severe Asthma in Ontario, Canada from 2003 to 2009</td>
<td>e66</td>
</tr>
<tr>
<td>Wickerson, Lisa</td>
<td>Functional Outcomes Pre- and Early Post-Lung Transplantation</td>
<td>e77</td>
</tr>
</tbody>
</table>
Basic Science / Science fondamentale

1

GROWTH-RELATED ONCOGENE (GRO-α) INHIBITION OF AIRWAY SMOOTH MUSCLE CELL REMODELING IS MEDIATED BY THE DECOY RECEPTOR ‘DUFFY ANTIGEN RECEPTOR FOR CHEMOKINES’ DARC

L Al-Alwan1, Y Chang1, C Baggole1, A Halayko2, JG Martin1, DH Eidelman1, Q Hamid1

1Meakins-Christie Laboratories and Respiratory Division, Department of Medicine McGill University, Montreal, Quebec; 2The Department of Physiology, University of Manitoba, Respiratory Hospital, Winnipeg, Manitoba

RATIONALE: Cell migration is an important biological mechanism that is involved in the pathophysiology of several diseases, such as asthma. Chemokines and their receptors are essential for induction of inflammation in the diseases, and structural cell migration. We previously established that IL-17 induced growth-related oncogenes (GROα, GROβ and GROγ) can promote human airway smooth muscle cell (ASM) migration in an autocrine fashion. This effect was mediated through their putative receptor, the CXCR2 receptor. In this study we aimed to investigate the particular effects of GRO-α on ASM migration and the mechanism(s) by which this migration is mediated.

METHODS: High-fold concentrations (0.01, 0.1, 1, 10 and 100 ng/ml) and low-fold concentrations (0.25, 0.5, 1, 2 and 4 ng/ml) of recombinant human GRO-α were used to assess ASM migration using a modified Boyden chamber. The mechanism by which GRO-α regulates ASM migration was investigated, firstly; by assessing the receptor(s) mediating this effect either by use of neutralizing antibodies or siRNA knock-down and secondly; by utilizing pharmacological inhibitors we examined the signaling pathways activated by these receptors.

RESULTS: At high-fold concentrations GRO-α has no effect on ASM migration; however, when using the low-dose concentrations, at 2 and 4 ng/ml, GRO-α appeared to exhibit an inhibitory effect on ASM migration. When investigating the receptor mediating the inhibitory effect of GRO-α on ASM migration, we found it to be mediated through the decoy receptor ‘Duffy antigen receptor for chemokines’ (DARC), but not CXCR1 nor CXCR2. Finally, we established ERK 1/2 MAPK as the signaling pathway responsible in mediating GROα inhibition of ASM migration

CONCLUSION: Unlike the common notion of chemokines function as inducers of cell migration, we established GRO-α as a negative regulator of ASM migration. An effect that was mediated DARC receptor and ERK 1/2 MAPK pathway. These results suggest that GRO-α/DARC axis may be a potential target of therapy in diseases where inordinate cell migration plays a central role.

2

CT-ANGIOGRAPHS AND PULMONARY VASCULAR REMODELING IN PULMONARY ARTERIAL HYPERTENSION

Barrier Marjorie, Courboun Audrey, Tremblay Eve, Chapalard Mathilde, Jacob Maria-Helena, Bissier Malik, Lambert Caroline, Loeher Jérémie, Roy Marie-Claude, Tremblay Véronique, Provencal Steeve, Bonnet Sébastien

Centre de recherche de l’Institut universitaire de cardiologie et de pneumologie de Québec, Université Laval, Québec, Québec

RATIONALE: In pulmonary arterial hypertension (PAH), distal pulmonary arteries (PA) are remodelled, which elevates pulmonary vascular resistance (PVR), decreases blood lung perfusion, and leads to fatal right ventricular (RV) heart failure. Current treatments are not efficient and don’t target PA remodeling processes. CT-angiography could be an efficient tool to assess pulmonary perfusion and thus pulmonary vascular remodeling in both PAH animals models and PAH patients.

METHODS/RESULTS: Pulmonary CT-angiograms were performed in chronic hypoxia (CH), monocrotaline (MCT) and Sugen5416 (SU5416) rats, with respectively limited, medium and severe vascular remodeling. The total lung perfusion decreases with histologically assessed PA remodeling severity (r2=0.9932; p=0.0526). Indeed, the CH model has a small decrease in perfusion (63.19%; n=4), the MCT model has a moderate one (53.47%; n=13, p<0.001) and the SU5416 model an even more important decrease (44.16% n=4, p<0.001) compared to control rats. The decrease in lung perfusion is due to remodeling of the distal PA averaging a size of 200 to 300 μm in the MCT and 200 to 500 in the SU5416 model (p<0.05). In addition, we established that lung perfusion assessed by CT-scan correlates with other PAH severity-related parameters including mean PA pressure and PVR (right heart catheterization), pulmonary artery acceleration time (echo-Doppler) and RV hypertrophy (echo), (p≤0.001 and respectively: r=-0.5562, n=43; r=-0.7345, n=41; r=0.6318, n=50; r=-0.6125, n=50).

Finally, we established that CT-angio represents an efficient way to study longitudinally follow-up treatment efficiencies in both MCT and SU5416 models. We were also able to analyze PAH patients’ pulmonary angiograms using the same calculation technique.

CONCLUSION: Pulmonary CT angiogram represents a powerful tool in assessing pulmonary vascular remodeling in preclinical tests and could be used in future clinical trials as well.

Fundings: MB has an SQHA funding and SB has a CIHR grant.

3

GENETIC DELETION OF IL-17 AMELIORATES INFLAMMATORY RESPONSE AND AIRWAY REMODELING IN A MOUSE MODEL OF CHRONIC SEVERE ASTHMA

Y Chang1,*, L Al-Alwan1,*, J R Johnson1, S Audusseau1, C Baggole1, DH Eidelman1, Q Hamid1

1Meakins-Christie Laboratories and Respiratory Division, McGill University Health Centre and Department of Medicine McGill University, Montreal, Quebec. *These authors contributed equally to the work

RATIONALE: Asthmatic airway remodeling, the pathophysiological modifications of the normal airway wall structure, is the major cause of the symptoms associated with decreased pulmonary function. The IL-17 superfamily, which mediates cross-talk between the adaptive and innate immune systems, has been associated with severity of disease. To explore the roles of IL-17 in airway remodeling of asthma, we used a model of severe asthma driven by chronic respiratory exposure to house dust mite (HDM) exposure in wild type and IL-17 deficient mice.

METHODS: Male and female C57BL/6 mice (6-8 weeks old) and IL-17-/- mice (C57BL/6 background) were exposed to purified HDM extract intranasally for 5 days/week for 5 consecutive weeks. Sterile saline was used as the control. Airway responsiveness was measured on the basis of the response of the total respiratory system resistance to increasing doses of methacholine. The inflammatory cells in bronchoalveolar lavage fluid (BALF) were counted. Airway smooth muscle bundle and collagen deposition were observed respectively by anti-smooth muscle actin immunohistochemistry and Picro Sirius red staining. The level of IL-17A, IL-4, IFN-γ and KC in BALF was assayed by Bioplex system.

RESULTS: The expression of IL-17A increased in wild type (WT) mice with HDM exposure (9.8 fold increase compared to the control mice). The deficient of IL-17 was not able to reduce the AHR induced by HDM exposure. In comparison to HDM exposed WT mice, BALF neutrophils in IL-17-/- mice were significantly decreased. In WT mice, HDM exposure led to increased expression of IL-4 and KC, which was significantly decreased in IL-17-/- mice. Furthermore, under HDM exposure, significantly less of airway smooth muscle mass and collagen deposition was found in IL-17-/- mice compared to WT mice.

CONCLUSIONS: Taken together, these findings suggest that IL-17 plays an important role in the inflammatory response to HDM exposure through increased expression of KC and Th2 cytokine IL-4. Moreover, IL-17 may also contribute to increased airway smooth muscle mass and collagen deposition found in asthma. This study suggests that IL-17 may have a critical role in the inflammatory reaction and airway remodeling in asthma.

Can Respir J Vol 20 No 3 May/June 2013 e63

Abstracts
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4 EXPRESSION QUANTITATIVE TRAIT LOCI (EQTL) MAPPING OF THE MAJOR HISTOCOMPATIBILITY COMPLEX IN HUMAN LUNG
Maxime Lamontagne1, Christian Couture1, The Merck-Laval-UBC-Groningen Lung eQTL consortium, Michel Laviolette1, Yohan Bossé1,2
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The major histocompatibility complex (MHC) is a key region in the human genome for the immune system. The extended MHC in human (xMHC) covers 7.6 Mb on the short arm of chromosome 6. Variants in MHC genes are associated with hundreds of diseases, particularly autoimmune diseases. The genetic mechanisms regulating the MHC complex are still unclear. The lungs are extensively exposed to environmental pathogens and are the most common route of infections. The MHC is thus a critical genomic region to control infections in the lung such as pneumonia and tuberculosis. The MHC is also known to play a critical role in the development of chronic lung diseases (eg, COPD and asthma). The goal of this study is to further our understanding of the mechanisms regulating this important region by using lung expression Quantitative Trait Loci (eQTL). Genome-wide gene expression profiles of 500 non-tumor lung specimens were obtained from patients undergoing lung surgery. Blood-DNA from the same patients were genotyped for 1,2 million SNPs. Following genotyping and gene expression quality control filters, 409 samples were analyzed. A large number of eQTLs was identified in the xMHC compared to other genomic regions of the same size. The expression of a number of genes were regulated by multiple independent SNPs. Notably, the expression of HLA-DRB5 was regulated by more than 20 SNPs. rs35366052 was the most significant SNP regulating the expression of HLA-DRB5 (p = 2.488E-297). Regulatory genetic variants were also found to be pleiotropic. For example, rs2647012 located in the HLA-DQ loci was significantly associated with the expression of 6 genes. This study is important in increasing our understanding of the genetic mechanisms regulating the MHC region and its role in pulmonary infections and chronic respiratory diseases.

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5 THE ADVANCED GLYCATION ENDPRODUCTS RECEPTOR: NOVEL THERAPEUTIC TARGET OF PULMONARY ARTERIAL HYPERTENSION
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RATIONALE: Pulmonary arterial hypertension (PAH) is characterized by enhanced vascular remodeling and pulmonary pressure. Pulmonary artery smooth muscle cells (PASMC) play a crucial role in vascular remodeling because of their high proliferative rates and suppressed apoptosis. This PAH-PASMC phenotype is very similar to cancer cells. Recent studies showed that some proteins implicated in cancer are also implicated in PAH. The receptor of advanced glycation endproducts (RAGE) is implicated in cancer progression by enhancing proliferation and migration. Recently, a proteomic analysis of PAH lungs versus healthy lungs demonstrated that RAGE is one of the most upregulated proteins in PAH patients. We thus hypothesized that RAGE could play a critical role in PAH etiology and progression.

METHODS/RESULTS: We demonstrated a specific RAGE overexpression in PAH lungs (qRT-PCR; n=6, p<0.05). In human PASMC (from healthy donors and PAH patients), we showed that RAGE was implicated in the proliferative and apoptosis-resistant phenotype (Ki67 and TUNEL assays, n=3 to 5, p<0.05). Recent studies demonstrated an altered BMPR2 (Bone Morphogenetic Protein Receptor 2)/PPARγ (Peroxisome Proliferator-Activated Receptor gamma) axis in PAH. We showed for the first time that RAGE was responsible of BMPR2/PPARγ downregulation, thus regulating proliferation and apoptosis (immunoblot, qRT-PCR, immunofluorescence, n=5, p<0.05). In vivo, RAGE inhibition (siRNA nebulization) in rats with Sugen-induced PAH showed decreased PA pressure and right ventricular hypertrophy (catheterization and echocardiography, n=8 per group). This was associated with a significant improvement in lung perfusion and decreased PA wall thickness (CT-scan, H&E; n=8, p<0.05).

CONCLUSION: We demonstrated that RAGE is implicated in PAH etiology and RAGE inhibitors, which are in clinical phase II for Alzheimer’s disease, represent potential therapeutic agents for PAH treatment.

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THE QUEBEC CITY CASE-CONTROL ASTHMA COHORT
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INTRODUCTION: One of the main challenges of genetic research is our ability to access large samples including subjects well characterized for the disease of interest.
OBJECTIVE: Here, we describe the collection of the Quebec City Case-Control Asthma Cohort. This cohort is part of an ongoing project initiated in 2007 to elucidate the genetic basis of asthma.
METHODS: All subjects are recruited at the respiratory unit of the Institut universitaire de cardiologie et de pneumologie de Québec (IUCPQ), Québec, Canada. Subjects are randomly included following advertisements and DNAs from patients with or without asthma are collected. Each participant undergoes a spirometry, methacholine challenge, allergy skin-prick tests and total serum IgE measurement. Airway hyperresponsiveness (AHR) is defined as a provocative dose of methacholine lower than 8 mg/ml inducing a 20% fall in forced expiratory volume in one second (FEV1).
RESULTS: So far, 872 subjects have been recruited including 490 cases and 382 controls. More females (n=557) than males (n=315) were enrolled, but the proportion of men and women is similar between cases and controls. These subjects are all unrelated French Canadian white adults 18 years of age or older. A greater proportion of young adults (20 to 30 years) is observed. As expected, predicted lung functions are lower in asthmatic subjects (FEV1 = 91.2±17.4 vs 105.3±13.6). 82% of asthmatics and 88% of non-asthmatic subjects and controls have allergies, respectively. Blood eosinophils and total IgE levels are higher in asthmatics.
CONCLUSION: The Quebec City Case-Control Asthma Cohort will power our own genomic research program on asthma. This cohort will also elucidate the genetic basis of asthma.

8
IMPORTANCE OF IDENTIFYING BODY DISTRESS IN PATIENTS WITH SEVERE ASTHMA– A CASE SERIES
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RATIONALE: Many studies have shown a positive association between psychological distress and severe asthma. Despite growing emphasis on incorporating psychological therapies into standard medical treatments, the mechanics of such therapies have not been addressed.
CASE SERIES: Three patients referred to the Refractory Asthma Clinic for uncontrolled asthma continued to experience persistent respiratory symptoms requiring emergency room (ER) visits despite intensive investigations and aggressive medical therapy. These patients exhibited a number of psychobiologic attributes consistent with body distress (dysfunctional breathing, body guarding, fatigue, Type A personality, non-restorative sleep, musculoskeletal pain, abuse history) and were referred to the Clinic for Mind Body Medicine. They were individually instructed in somatic awareness techniques including autogenic relaxation and effortless breathing. All of the patients achieved well-controlled asthma symptoms within 3 months with no ER visits and a reduction in Salbutamol use from up to 20 inhalations/day to less than 2 inhalations/week.

DISCUSSION: Severe asthma self-management can be enhanced by characterizing psychological influences as psychobiologic rather than mental in origin and function. Somatic awareness, a normal property of consciousness, serves to network the physiological, psychological, and contextual variables unique to each patient that needs to change. Interventions include effortless breathing, autogenic relaxation and body mindfulness – all of which are used to guide the patient to interoceptive experiences and associated feelings for the purpose of asthma self-management.
CONCLUSION: Unrecognized body distress may be a clinically important factor in the overreliance on high doses of inhaled and systemic corticosteroids and dependence on rapid-acting bronchodilators by uncontrolled asthmatics. Developing somatic awareness as a transformational wellness skill represents a new paradigm for many severe asthma patients who have believed, to this point, that body experiences outside of worsening asthma symptoms are to be ignored.
Financial Support: None

10
LUNG FUNCTION ASSOCIATED WITH CHRONIC CONDITIONS AMONG THOSE WITH AND WITHOUT ASTHMA OR COPD
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BACKGROUND AND RATIONALE: Some chronic conditions may result from similar mechanisms suggesting the investigation of disease inter-relationships. We sought to determine if lung function indices differed among adults with and without chronic conditions particularly in those individuals with and without asthma or COPD.
METHODS: We conducted a cross-sectional survey as part of the Saskatchewan Rural Health Study in 2010. Questionnaires were mailed to households in rural Saskatchewan. One adult per home provided information regarding each adult living in the home. There were 8261 adults from 4624 households included. Using descriptive statistics and multiple logistic regression, we examined the associations between reported diagnosed chronic conditions (diabetes, cardiovascular conditions, chronic bronchitis, and sleep apnea) and lung function indices (FEV1, FVC, FEV1/FVC, FEF25-75) after adjusting for potential confounders and stratifying by history of doctor-diagnosed asthma or COPD.
RESULTS: The respondents’ mean age was 56 years (SD=16 years) with 51% of the population being female. After adjustment, the subjects with no history of asthma or COPD had significantly lower FVC and FEV1 values associated with diabetes (−0.17 l, −0.22 l), cardiovascular disease (−0.09 l, −0.15 l), and chronic bronchitis (−0.13 l, −0.15 ) but not sleep apnea. Among those with a history of asthma or COPD, only those individuals whom had diabetes had significantly lower FEV1 (−0.53 l).
CONCLUSIONS: Cardiovascular disease and chronic bronchitis were associated with lower lung function in the absence of asthma or COPD. Diabetes was associated with lower FEV1 both in the presence and absence of asthma and COPD, with corresponding lower FEV1 levels in the presence of asthma/COPD. A non-respiratory chronic condition and lower lung function may result from common pathways, possibly inflammatory in nature, and may precede more serious chronic lung disease.
Financial Support: Canadian Institutes of Health Research (MOP: 90002)
Abstracts

11

RELATIONSHIP BETWEEN AIRWAY HYPERRESPONSIVENESS AND CLINICAL ASTHMA IN MORBIDLY OBESE PATIENTS
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RATIONAL: Although there seems to be an association between obesity and self-reported asthma symptoms, an objective biologic causality still remains to be proven. In fact, over diagnosis of asthma in obese patients complaining of shortness of breath represents an epidemiological problem.

OBJECTIVES: In a morbidly obese population, we investigated the relationship between airway hyperresponsiveness (AHR) and 2 factors: having a clinical diagnosis of asthma or taking any asthmatic medication.

METHODS: All subjects over 18 years old, with morbid obesity (BMI > 35 kg/m²), awaiting a bariatric surgery and referred systematically for a presurgery assessment, including a metacholine challenge test, from 2001 to 2010 at Sacré-Coeur Hospital, were included in the analysis. A FEV1 fall of 20% or more (PC20), at a metacholine concentration of less than 8 mg/ml, was considered a positive result for AHR. The Cohen’s Kappa Coefficient (k) was used to assess the agreement between having AHR and having a diagnosis of clinical asthma or taking any asthmatic medication, these information having been found in the patients’ medical files.

RESULTS: A total of 286 patients awaiting bariatric surgery, with a mean age of 41.6 ± 10.7 years (28.8% males), were included in the analysis. Among those morbidly obese patients, 69 subjects (24.1%) had a PC20 ≤ 8 mg/ml. The Kappa Correlation Coefficient between having a PC20 ≤ 8 mg/ml and the diagnostic of asthma or taking any asthma medication was 0.33 (CI 95% 0.18-0.43), demonstrating a weak relationship between the clinical diagnosis of asthma and the objective measure of AHR.

CONCLUSION: In our cohort of morbidly obese patients, having a PC20 ≤ 8 mg/ml was only weakly correlated with a clinical diagnostic of asthma and emphasized the hypothesis that the mechanical effects of obesity on lung volumes can explain the presence of AHR in this population.

12

THE PREVALENCE OF SEVERE ASTHMA IN ONTARIO, CANADA FROM 2003 TO 2009
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RATIONAL: Individuals with severe asthma may be predisposed to exacerbations, emergency department (ED) visits, hospitalization and death. Understanding population trends of severe asthma and identifying at-risk groups may help in targeting asthma management strategies to reduce morbidity.

METHODS: Applying a validated case definition using provincial population-based health administrative data, the Ontario Asthma Surveillance Information System (OASIS) identified and followed approximately 1.7 million prevalent asthma cases from 2003 to 2009. The severity of prevalent asthma was classified into intensive care unit (ICU) admission, hospitalization, and multiple ED visits based on events that occurred in the 12 months of each year. The prevalent cases by these severity categories were described by age, sex, urban/rural residence and socioeconomic status.

RESULTS: Hospitalizations decreased from 3.76 in 2003 to 2.18 per 1,000 population in 2009, and multiple ED visits decreased from 3.96 in 2003 to 2.33 per 1,000 population in 2009 (see Figure). Young children and older adults were more likely to be admitted to the ICU. The prevalence of hospitalizations and multiple ED visits had a bimodal distribution with the highest peak in young children and a second peak in young adults aged 20-39 years. Overall, the prevalence of all severity categories was highest in the lowest income quintile, and multiple ED visits were twice as prevalent in rural regions compared to urban areas.

Clinical, COPD/Recherche clinique, MPOC

13

THE PREVALENCE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) IN INDIVIDUALS WITH DIABETES, HYPERTENSION, ASTHMA OR MOOD/ANXIETY DISORDERS: A CANADIAN POPULATION STUDY
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RATIONAL: There is little information on the prevalence of COPD among people with other chronic conditions. We determined the cross sectional prevalence of COPD among Canadians with diabetes, asthma, hypertension, and mood/anxiety disorders. We also compared the all-cause mortality between individuals with these other diseases with/without COPD.

METHODS: Using the Canadian Chronic Disease Surveillance System (CCDSS), we analyzed 2008/2009 administrative health data for Canadians aged 35 years and older, from 12 of 13 provinces/territories. COPD, diabetes, mood/anxiety disorders and asthma were identified using ICD9/10 codes from physician billing and hospitalization records.

RESULTS: The prevalence of COPD among Canadians aged 35 years and older was 8.2%. The prevalence of COPD among people with diabetes, hypertension, asthma or a mood/anxiety disorders was respectively 11.4% (95% confidence interval (CI) 11.35, 11.44), 10.0% (95% CI 9.99, 10.04); 11.6% (95% CI 11.57, 11.66) and 26.3% (95% CI 26.20, 26.35). In addition, a diagnosis of COPD was associated with a 140% increase in mortality among people with diabetes and a 154% increase in mortality among those with hypertension.

CONCLUSIONS: COPD is a prevalent comorbid condition for individuals 35 years of age and older affected with chronic diseases, particularly those with asthma or a mood/anxiety disorders. Moreover, comorbid COPD is associated with higher mortality. An integrated care approach to
these patients may optimize health outcomes and reduce the burden of chronic disease.

Financial Support: Funding and support in kind was provided by The Public Health Agency of Canada.

14 MOBILITY AND PHYSICAL FUNCTION IN HOSPITALIZED PATIENTS WITH AN ACUTE EXACERBATION OF COPD

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RATIONALE: There is little information on the characteristics of physical inactivity in individuals hospitalized with an acute exacerbation of COPD (AECOPD). We investigated the mobility, six minute walk distance, 4 meter gait velocity and daily average metabolic equivalents (METS) in patients hospitalized with an AECOPD.

METHODS: We recruited hospitalized AECOPD patients who were greater than 35 years old; had spirometric/physician diagnosis of COPD; and were not on bedrest. We assessed six minute walk distance (6MWD), gait velocity, and mobility using the De Morton Mobility Index (DEMMI) and daily average METS using an activity monitor, on Day 3 and/or Day 6 of their admission.

RESULTS: Twenty participants (60% male) were recruited between April-October 2012. Participants were 62 (±12) years, with 39 (±21) pack years of smoking history and a body mass index of 28 (±10) kg/m2. Fourteen individuals had Day 3 measures. The mean (SD) 6MWD was 224 (99) meters. The mean gait velocity was 5.6 (1.6) seconds. The mean METS expended over the 24 hour monitoring period was 1.2 (0.29). The mean DEMMI score was 74/100 (20). The most affected attribute of mobility was balance – only 20% of participants achieved a perfect balance score while 80% of the participants achieved a perfect walking score. The correlation between the Day 3 DEMMI score and 6MWD was r=0.72 (p=0.004) and between the DEMMI and the gait velocity was r=-0.54 (p=0.045). There was no relationship between the DEMMI score or the 6MWD and the mean METS.

CONCLUSIONS: Hospitalized AECOPD patients have reduced mobility, mainly due to poor static and dynamic balance. The daily average energy expenditure had no relationship with walking capacity or mobility, indicating that other factors contribute to physical inactivity in these patients.

Financial Support: Funding was provided by Canadian Respiratory Health Professionals and the Physiotherapy Foundation of Canada.

15 ACTIGRAPHIC ASSESSMENT OF SLEEP PARAMETERS IN COPD IN RELATION TO ANXIETY AND DEPRESSION SYMPTOMS

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RATIONALE: Anxiety and depression have been shown to be highly prevalent in chronic obstructive pulmonary disease (COPD). A two-way relationship exists between sleep quality and mood disorders, and actigraphy can estimate the quality of the sleep-wake cycle. The objective was to determine if the quality of the sleep-activity cycle was associated with depression and anxiety symptoms in COPD.

METHODS: Depression and anxiety symptoms were assessed using the Center for epidemiologic studies in depression and the Beck anxiety questionnaire. Subjects were instructed to wear an ambulatory activity monitor (Actiwatch-L, Mini-Mitter/Respiriconics, Bend, OR, USA) over 24 hours, for 7 consecutive days. The Actiwatch was worn on the non-dominant wrist and recorded activity on a minute-by-minute basis. The Actiware software estimated the amount of time asleep at night and in the daytime. Sleep efficiency (% time asleep/time in bed) was calculated as an estimate of night-time sleep quality. Correlation analyses were conducted between depression and anxiety scores and rest-activity parameters.

RESULTS: Fourteen subjects (nine male) with moderate to severe COPD completed the study (FEV1: 58±13% predicted). Scores for depression averaged 12.07±9.74 with a range of 2-27, while anxiety scores averaged 9.21±6.86 with a range of 1-24. Patients spent almost 8 h in bed at night (476.5±54 min). Sleep efficiency was estimated as 81.2% (± 8%). A large amount of sleep was observed in the daytime (3.2 h), with high variability between subjects (SD=100.4 min). The estimated measures of sleep quantity and quality were not significantly correlated with anxiety or depression scores.

CONCLUSION: No overall correlation was found between the actigraphic sleep measures and depression and anxiety scores in the present study.

FINANCIAL SUPPORT: JW McConnell Graduate Memorial Scholarship

16 A DECADE OF QUALITATIVE RESEARCH IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): A META-METHOD STUDY

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RATIONALE: There is a large body COPD evidence. In particular to COPD qualitative evidence, varied theoretical and methodological approaches have been used to reveal a range of experiences and perceptions from samples of patients, their families and/or health care providers. This has resulted in diversity of findings within a specific topic domain such as end-of-life care and experience of acute exacerbations of COPD and dyspnea. As a result, navigating through multiple, and at times, divergent findings may pose challenges for clinicians wanting to utilize evidence in practice.

AIM: This meta-method study is a component of a part of a larger meta-study focused on the strengthening of COPD services from the perspectives of patients, families and health care providers. By understanding the epistemological and methodological issues underpinning the findings, we are able to consider how the methodology that has been applied to the generation of knowledge in the area of COPD evidence has shaped current understandings about it (Paterson et al., 2001).

METHODS: The design of this study was meta-method. According to Paterson and associates (2001) meta-method is a systematic process involving the examination and aggregation of methodological features across qualitative reports for the purpose of understanding the quality of the findings. Searching computerized academic data bases, 61 reports were included. These were English written reports published between 2001 and 2013 that used a qualitative approach and involved participants as either users or providers of COPD services.

RESULTS: Across the 61 reports, findings of the meta-method revealed at least 39 (64%) of the qualitative evidence was published in the past 5 years. The majority of the COPD evidence, 15 of the 61 reports (25%), originated in Canada and the primary authors of many of the studies were most often from the discipline of nursing (64%).

CONCLUSION: A systematic approach and critical appraisal of the COPD evidence is essential in order to describe the soundness of this body of research. In doing so, health care professionals are better able to utilize evidence in their practice that is rigorous and sound.

17 CHANGES IN EXERTIONAL DYSPNEA AFTER SINGING INTERVENTION IN PULMONARY REHABILITATION ATTENDEES

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RATIONALE: Exertional dyspnea is one of the biggest...
issues in pulmonary rehabilitation attendees. The majority of attendees in pulmonary rehab have a diagnosis of COPD. During exercise in people with COPD, dyspnea increases due to lung hyperinflation. It is hypothesized that regular singing lessons will increase breathing control and inspiratory capacity, leading to decreased hyperinflation.

METHODS: Ten subjects attending pulmonary rehabilitation were enrolled in the study (avg age 67.9, 6 males, 4 females). Eight of the subjects had a diagnosis of COPD, one with interstitial lung disease, and one with a lung transplant. The intervention consisted of eight weekly structured singing classes involving upper extremity and neck stretches, breathing exercises, vocal warm-ups, and group singing. Each participant completed spirometry, incremental shuttle walk test (ISWT), and endurance shuttle walk test (ESWT) both before and after participation in the group (except ISWT).

RESULTS: Data was analyzed for 7 of the 10 subjects, as 3 of the subjects had anomalous test results. There was no significant change in ESWT time or in spirometry results from pre to post. Peak exertional dyspnea was decreased (p<0.01), as well as peak respiratory rate (p<0.05) from pre to post singing ESWT. Against expectations, peak IC (p=0.201) and peak ventilation (p<0.05) were both decreased. Percent change in shortness of breath from pre to post during ISWT was positively correlated with percent change in peak tidal volume (p<0.05). There was a trend towards an increase in peak tidal volume from pre to post, which did not reach statistical significance.

CONCLUSION: There is preliminary data to indicate that a singing intervention may lead to a decrease in perceived exertional dyspnea.

18 MEASUREMENT OF ACTIVITIES OF DAILY LIVING IN COPD: A SYSTEMATIC REVIEW
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RATIONALE: In chronic obstructive pulmonary disease (COPD), limitations during activities of daily living (ADL) have been found to be a predictor of mortality. Despite its importance, current international guidelines in COPD do not include measurement of ADL as a recommended outcome nor make any mention on how to measure it in a clinical or research setting. The objectives of this study were: (i) to synthesize the literature on measures of ADL that have been used in individuals with COPD and (ii) to provide an overview of the psychometric properties of the identified measures that have been evaluated in COPD.

METHODS: Studies conducted in individuals with COPD that included a measure of ability to perform ADL were identified after searches of 5 electronic databases and reference lists of pertinent articles. Key terms included: COPD, activities of daily living, daily activities, day to day activities, daily life activities, tool, measure, instrument, test, questionnaire, scale, assessment and outcome. One reviewer performed the data extraction and tabulation using a standardized form.

RESULTS: Of 668 articles, 117 met the study criteria. Thirty ADL tools were identified among the studies. Of those, 12 tools were respiratory disease-specific while 18 were generic ADL tools. The majority of the tools were interview-based or self-reported questionnaires. Only three tools were performance-based tests and of these, only one was specifically developed for individuals with COPD. Twenty-four studies assessed validity and reliability of respiratory disease-specific ADL tools in COPD and of those, only five evaluated responsiveness. No study assessed interpretability of ADL measures in COPD.

CONCLUSIONS: Although there are respiratory-disease specific tools available, many studies have used generic ADL tools that are not validated for COPD. There is a lack of performance-based tests to assess ADL in COPD. More research on psychometric properties of ADL tools used in COPD is needed.

Financial Support: ORCS and CRHP.

19 PREVALENCE AND PROFILE OF PATIENTS WITH A DIAGNOSIS OF COPD PARTICIPATING IN NON-PULMONARY REHABILITATION PROGRAMS
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RATIONALE: The aim of this study was to determine the prevalence of patients with a primary or secondary diagnosis of COPD among individuals who completed a non-pulmonary rehabilitation program and to describe the clinico-epidemiological profile of these patients.

METHODS: Retrospective electronic data review of 1793 patients who completed a non-pulmonary inpatient rehabilitation program at the St John’s Rehab program of Sunnybrook Health Sciences Centre between July 1st 2010 and March 31st 2011. Gender, age, primary or secondary diagnosis of COPD, reason for admission, most responsible health condition, type of program completed, length of stay and functional independence measure (FIM) on admission and discharge were collected.

RESULTS: One hundred thirty-seven patients (80 women [58.4%] and 57 men [41.6%]) were identified with a primary (10%) or secondary (90%) diagnosis of COPD. Mean (SD) age was 75 (11). The majority of the patients participated in the musculoskeletal inpatient program (n=63; 46%). Other types of programs were: (i) Cardiac (n=27; 20%); (ii) Complex care (n=23; 17%); (iii) Neuro (n=8; 6%); (iv) Amputee (n=7; 5%); (v) Transplant (n=6; 4%) and (vi) Trauma (n=3; 2%). The most common reason for admission was “status post unilateral hip replacement” (n=24). The mean (SD) length of stay was 22 (16) days. The mean (SD) of the FIM on admission and discharge were 93 (10) and 109 (7) respectively.

CONCLUSIONS: The prevalence of patients with COPD was 7.6%. COPD is a common comorbidity among patients admitted for musculoskeletal rehabilitation. In order to optimize the management of patients with COPD enrolled in other rehabilitation programs, it would be worthwhile introducing COPD-specific interventions.

Financial Support: St. John’s Rehab Foundation.

20 EXPLORING THE PERSPECTIVE OF HEALTHCARE PROFESSIONALS ON THE INITIATION OF ADVANCE CARE PLANNING DISCUSSIONS WITH COPD PATIENTS AND THEIR FAMILIES
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BACKGROUND: Chronic Obstructive Pulmonary Disease (COPD) is a disease with an increasing prevalence and a unique illness trajectory. Even though latest evidence highlights the need to initiate Advance Care Planning (ACP) discussion early in the course of the disease, the practice does not yet consistently match these requirements. Many barriers to discussion have been identified and HCPs are looking at how to overcome them.

OBJECTIVE: The purpose of this study is to explore how the beliefs and values of HCPs influence their initiation of ACP discussion with COPD patients and their families. This study is intended to follow on the recent work done by Nguyen et al. (2012) examining the beliefs and perceptions of COPD patients with regards to ACP discussions.

METHODS: A qualitative descriptive design was used to gather meaningful data from 13 HCPs. Three physicians, five nurses, and five registered respiratory therapists (RRTs) working at the Montreal Chest Institute (MCI) were purposefully selected based on their experience in caring for COPD patients. The participants each took part in a semi-structured interview.

RESULTS: Early analysis shows the understanding of the concept of ACP is still highly associated with code status discussion. Although all
procedures agree that ACP discussions should be performed in an inter-disciplinary fashion, there is no clarity on the roles and responsibilities of each professional group, patients, and families in the process. Multiple beliefs seem to be implicated in the approach to and the ability to open discussions. While most professionals state they separate their values from their practice, many have been conflicted with the distress of the struggle.

**CONCLUSION:** It appears that HCPs need guidance in comprehending the scope of their role and responsibilities in the discussion process. Moreover, interprofessional education is warranted to increase understanding of ACP and address the various beliefs of HCPs.

Financial Support: None

### 21

**RELATIONSHIP BETWEEN ACUTE AFFECTIVE AND SYMPTOMATIC RESPONSES TO EXERCISE TRAINING AND COMPLIANCE TO PULMONARY REHABILITATION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE**

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**RATIONALE:** We recently reported that affect improved after an exercise-training bout in patients with chronic obstructive pulmonary disease (COPD), regardless of the training protocol utilized. However, training at the ventilatory threshold (CTVT) was associated with better vigor and less leg fatigue end-exercise than interval (IT) or continuous high-intensity training (CTHT). The objective of the present study was to investigate whether acute affective and symptomatic responses to exercise training were associated with subsequent compliance to a 12-week pulmonary rehabilitation program.

**METHODS:** Subjects were randomly assigned to CHTH, CTVT, or IT. Exercise interventions consisted of cycling on a leg ergometer for ≥40 minutes. Acute responses were measured during a single exercise-training bout at the beginning of the rehabilitation program. Affect was assessed using the Positive and Negative Affect Schedule (PANAS) and Global Vigor and Affect Instrument (GVA). Symptoms were measured using the modified 10-point Borg scale. Subjects subsequently trained three times weekly for 12 weeks. Compliance was measured with data tracking technology and defined as the percent time spent at the target heart rate throughout the 12-week program. Associations between a priori selected acute response variables and compliance were assessed using Pearson’s correlations.

**RESULTS:** Thirty-five COPD patients (FEV1 = 67.7±15.2 % predicted) completed the study. Compliance correlated positively with global vigor at 100% of exercise time (r=0.39, p=0.022) and negatively with leg fatigue at 100% of exercise time (r=-0.37, p=0.033).

**CONCLUSIONS:** These findings suggest that measures of global vigor and leg fatigue obtained during one exercise-training bout at the beginning of a pulmonary rehabilitation program may help predict subsequent program compliance in COPD patients.

**Financial Support:** This project was supported by the Fonds de recherche du Québec - Santé (FRQS), the Canadian Lung Association, and the Quebec Respiratory Health Training Program.

### 22

**THE IMPACT OF AIR QUALITY ON CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) MORBIDITY: A POPULATION-BASED STUDY**

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**RATIONALE:** Exposure to air pollution has been linked to the exacerbation of respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD). The goal of the study is to use an air quality health index to quantify the impact of air quality on COPD morbidity.

**METHODS:** Individuals aged 35+ who were diagnosed with COPD from 2003 to 2010 in Ontario were included. A previously validated COPD case definition is used: 1 or more COPD specific ambulatory claims and/or hospitalizations. The Air Quality Health Index (AQHI), developed by Health Canada and Environment Canada, is a health-risk scale for reporting air quality and advising risk reduction actions. AQHI measures were obtained from regional monitoring stations. For COPD specific or related conditions (acute bronchitis, pneumonia, influenza), hospitalization, emergency department (ED) and outpatient visit counts were obtained from a provincial registry of all individuals with COPD. Rate ratios (RR) from the Poisson regression models were used to estimate the impact of each incremental increase in AQHI on COPD-attributed health service use. We adjusted for age, sex, season, year, and region of residence.

**RESULTS:** For each unit increase in AQHI, there exist statistically significant increases in risk for ED visits (RR 1.028, 95% CI 1.025, 1.030; RR 1.042, 95% CI 1.040, 1.044) and outpatient visits (RR 1.051, 95% CI 1.050, 1.052; RR 1.017, 95% CI 1.016, 1.018) for COPD specific and related conditions respectively (see Figure).

**CONCLUSIONS:** Air pollution, as measured by the AQHI, was significantly associated with COPD health services use. Temply AQHI air quality advisories with integrated risk reduction messages may reduce morbidity associated with air pollution in individuals living with COPD.

**Funding Source:** Ministry of Environment, Government of Ontario

### 23

**LONG TERM HOME VENTILATION OF PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY**

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**RATIONALE:** Duchenne muscular dystrophy (MDM) is the most common form of muscular dystrophy. Non-invasive ventilation (NIV) is now widely used in supporting DMD patients. The Quebec National Program for Home Ventilatory Assistance (NPHVA) is a program that follows adult and pediatric patients who require home ventilation. The purpose of this report is to describe the experience of the NPHVA with DMD patients.

**METHODS:** We conducted a retrospective chart review of demographic data and ventilation delivery methods used for DMD patients followed by the NPHVA. This was approved by our Research Ethics Board (REB).

**RESULTS:** Currently, 28 patients are followed by NPHVA. The diagnosis of DMD was done primarily by the referring center either clinically with high creatine kinase (CK) with abnormal muscle biopsy, or by genetic studies. The median duration of ventilation is 5.7 years. Pulmonary function assessment: Median vital capacity (VC) at initiation was 0.74 L that decreased to 0.49 L on last available visit. PCO2 was 50.9 mmHg at initiation while it...
Abstracts

was 39.5 mmHg at last available visit. Ventilator settings: At initiation, 23 patients used bilevel positive pressure ventilation (Bilevel). 22 (96%) patients used spontaneous/timed (S/T) mode with a median Inspiratory Positive Airway Pressure (IPAP) of 14 cmH2O and Expiratory Positive Airway Pressure (EPAP) of 5 cmH2O. Another 4 patients used volume ventilation (VV) with an average tidal volume (TV) of 492 ml. On last visit, 21 patients used Bi-level ventilation. The main mode was again S/T with a median IPAP of 16 cmH2O and EPAP of 5 cmH2O. Among these, 3 patients used mouthpiece VV during the day, while using Bilevel at night. 5 patients used only VV with an average TV of 655 ml. One patient underwent tracheostomy.

CONCLUSION: Patients with DMD can be successfully ventilated non-invasively for many years with few changes to their ventilator settings.

Table: Ventilator settings at initiation and last visit

<table>
<thead>
<tr>
<th>Age (year)</th>
<th>Median Min Max n=</th>
<th>Median Min Max n=</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vital capacity (L)</td>
<td>18.8 13 30.2 28</td>
<td>23.95 16.9 45.5 26</td>
</tr>
<tr>
<td>PCO2 (mmHg)</td>
<td>50.9 38 66.5 27</td>
<td>39.5 33 77 18</td>
</tr>
<tr>
<td>Hours of use</td>
<td>8 8 24 28</td>
<td>13.5 8 24 26</td>
</tr>
<tr>
<td>Using &gt;16 h/day</td>
<td>1 (3.6%) 28 11 26</td>
<td>(42.3%)</td>
</tr>
</tbody>
</table>

No financial disclosure for all authors.

24 NEGATIVE PRESSURE WOUND THERAPY IN THE MANAGEMENT OF OPEN WINDOW THORACOSTOMY (THORACIC WINDOW)

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RATIONALE: Patients who experience prolonged weaning from mechanical ventilation (MV) have an increased risk of morbidity and mortality. Rehabilitation strategies directed at improving clinical outcomes among such patients are unknown.

METHODS: A retrospective review of rehabilitation received by patients admitted to a level 1 Critical Care Trauma Centre (CCTC) in London, Canada between March 1 and April 15, 2011 was conducted. Patients were included if they 1) were >18 years-old, 2) were ventilated for >48 hours, and 3) failed at least 3 attempts at liberation from MV or required >7 days of MV after the first liberation attempt.

RESULTS: Of the patients admitted to the CCTC within the 6 week period, 7/163 (4.3%) experienced prolonged weaning from MV. On average, these patients were elderly (median age 71y; range 26–86y) and severely ill (median APACHE III score 25, range 13-34). Patients had a median 24 days of MV (range 9-54) and most patients (6/7; 85.7%) were successfully liberated. One patient died after withdrawal from MV. All patients received physiotherapy which consisted of a combination of secretion mobilisation, airway clearance and lung expansion techniques, strengthening exercises and early mobility. The highest documented level of mobility at time of ICU discharge was standing (1/7; 14.2%), standing and transferring to a chair (3/7; 42.9%), and ambulating (3/7; 42.9%) with assistance. Documented morbidities during ICU stay included suspected ICU-acquired weakness (7/7; 100%), delirium (3/7; 42.9%), and joint contractures (1/7; 14.2%).

CONCLUSIONS: Patients who experienced prolonged weaning from MV were characterized by being elderly, severely ill, and having possible co-morbid conditions of ICU-acquired weakness, delirium and joint contractures. Most patients were successfully liberated from MV. All patients received regular physiotherapy.

Financial Support: none.
BREATHE: THE DEVELOPMENT OF A CANADIAN ASTHMA SELF-MANAGEMENT WEB APPLICATION

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RATIONAL: Asthma self-management is a key component of evidence-based care. Integration of personal health records from asthma data repositories into web-based applications accessible by clients may enhance self-monitoring and self-management, and improve patient outcomes.

METHODS: University Health Network’s Centre for Global eHealth Innovation, the Ontario Lung Association, clinical leads from University of Western Ontario and Queen’s University, TELUS Health Solutions, and Environment Canada worked collaboratively to develop the breathe application. Breathe was created using human factors engineering and user-centered design principles alongside Agile development and clinical content experts.

RESULTS: Development of a usable, useful, and engaging application.

conclusion: Breathe validated and strengthened the design, ensuring the development of a usable, useful, and engaging application.

Abstracts

METHODS: The base of our model was a plastic box, open on the top. Plastic supports projecting from the top of the box acted as a frame to give the artificial chest wall an appropriate convex shape. A thin adhesive film meant to imitate the parietal pleura was stretched over the plastic supports. Two pairs of fresh pork flank ribs were laid over the surface of the adhesive film. Once they were set in place, they were covered by a sheet of artificial silicone skin (Faux Medical®). This model was used to train 1st year surgery residents as part of their core surgical competencies course.

RESULTS: Chest wall thickness, resilience of muscle tissues, and the width and feel of intercostal spaces were all realistic. The adhesive film was a good imitation of the pleura, giving a satisfying "pop" as it was pierced with a hemostat or the operator’s finger. Digital probing of the "pleural space" through the incision provided convincing proprioceptive feedback. The artificial skin was replaced every one hour practice session while the rest of the model remained entirely usable throughout the four planned practice sessions. The total cost of our model was $205 compared to $1845 for the Life/form® manikin.

CONCLUSION: Our model is simple, inexpensive, and accurate, allowing to train residents in chest tube drainage.

Financial Support: This study was funded by a grant from the department of Surgery of the University of Montreal, Montreal, Canada.

28 BREATHING RETRAINING PROGRAM FOR HYPERVENTILATION SYNDROME

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BACKGROUND: Hyperventilation syndrome (HS) is a common disorder for which the treatment is usually breathing retraining. We evaluated the efficacy of our breathing retraining program (BRP) offered at Montreal Sacre-Coeur Hospital in the Respiratory Department.

METHODS: We conducted a retrospective study based on questionnaires filled out by patients from the breathing retraining clinic both previously and three months following the program. We used a questionnaire composed of 31 items (adapted from the Nijmegen questionnaire), with a score between 31 and 155 (a higher score being indicative of more severe symptoms).

RESULTS: 263 patients participated in the BRP between 2006 and 2011. Among those, 107 (40.7%) returned the post-treatment questionnaires (PTQ). A mean improvement of the total score by 23.1 points (p<0.001) was shown upon completion of the program. Using a ROC-curve, we determined that an improvement of the total score by 7 points would be significant, with a sensitivity of 83% and a specificity of 75%. 76.9% of patients improved their score by at least 7 points. Patients who returned PTQ were older (51.9 vs. 47.3 years old, p=0.018) and had followed the program for a longer time (3.6 vs. 2.7 sessions, p<0.001), and the cessation of treatment was more often determined by the respiratory therapist than by the patient alone (95 [88.8%] vs. 81 [51.9%], p<0.001).

CONCLUSION: Our BRP for HS appears to have improved symptoms in a large number of patients who returned PTQ. However, a significant proportion of patients did not return it, which limits our ability to conclude to the actual efficacy of our program. We will pursue this study by contacting these patients to better characterize them and to highlight determinants of a non-response to breathing retraining.

Funding: None.

29 SUPERVISED REGULAR EXERCISE AS AN AID TO SMOKING CESSATION: A STUDY OF THE QUIT & GET FIT PROGRAM

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BACKGROUND: Studies demonstrate that regular physical exercise can improve quit rates and reduce nicotine withdrawal symptoms and cravings. Since 2010, the Ontario Lung Association has partnered with the Ontario
Tobacco Research Unit to implement and evaluate the Quit & Get Fit (Q&GF) program aimed at assisting smokers to make quit attempts and successfully quit. In 2012, the program was offered in 28 community-based fitness facilities through personal trainers who attended the Q&GF online training. Participants completed 16 one-hour sessions of regular exercise and smoking cessation support over the course of 8 weeks. This poster presentation will discuss key evaluation findings and their implications for future program implementation.

METHOD: web-based baseline and follow-up surveys of participants; interviews with participants, personal trainers and program site coordinators

RESULTS: In 2012, a total of 193 female and male smokers aged 18 and above participated in the program. The self-reported 7-day point prevalence quit rate (intention-to-treat) was 39.4% at the end of program and 22.3% at 3 months follow-up. Participants who did not succeed in quitting were able to reduce daily cigarette consumption (from 15.2 to 10.9, \(P=0.001\)) and delay smoking their first cigarette of the day. However, their intentions to quit in the next 30 days decreased during and after the program. Both smokers and quitters reported higher levels of vigorous physical activity at the end of program (mean: 139.9 min/week) and 3 months follow-up (172.5 min/week) compared to baseline (67.2 min/week). Evaluation findings also indicate some challenges in program implementation and provide suggestions for improvements.

CONCLUSION: Q&GF is a promising intervention for promoting smoking cessation, reducing consumption of cigarettes and increasing engagement in physical activity. Evaluation findings support the need for further refinement of the intervention to increase the likelihood of successful quitting through regular exercise.

The program was led by the Ontario Lung Association and funded by the Government of Ontario.

30 EMERGENCY DEPARTMENT ASTHMA CARE PATHWAY INITIATIVE OF THE ONTARIO LUNG ASSOCIATION

Sandra Athron\(^1\), Diane Lougheed\(^2,3\), Jennifer Olajos-Clow\(^2,3\), Francine M Ducharme\(^4\), Mona Jabbour\(^5\)

\(^1\)Ontario Lung Association, Toronto; \(^2\)Kingston General Hospital; \(^3\)Queen’s University, Kingston, Ontario; \(^4\)Clinical Research Centre (Pediatrics) Centre hospitalier universitaire (CHU) Sainte-Justine, University of Montreal, Montreal, Quebec; \(^5\)University of Ottawa, Children’s Hospital of Eastern Ontario, Ottawa, Ontario

RATIONALE: A coroner’s inquest following an asthma-related teen death led to the Asthma Plan of Action (APA), an integrated Ontario asthma strategy. One of 13 APA initiatives, the Emergency Department Asthma Care Pathway (EDACP) initiative involved development and pilot evaluation of an evidence-based care pathway (CP) for acute asthma in adults (A) in Ontario emergency departments (EDs). Lessons learned from provincial implementation of the A-EDACP have informed revisions to the tools, and guided development of a Pediatric (P)-EDACP.

METHODS: The Ontario Lung Association assembled an interprofessional Steering Committee, and Adult and Pediatric Expert Content Working Groups to revise the A-EDACP and develop a P-EDACP. Incorporating similar tools and lessons learned from the adult pathway pilot project, development of a P-EDACP began in 2009. Key priorities were identified to guide deliberations, including: assessment of exacerbation severity; evidence-based treatment; patient education prior to discharge; comprehensive discharge instructions; and follow-up arrangements.

RESULTS: The revised A-EDACP (2012 version) includes simplified pre-printed orders (PPOs), medication guidelines, and discharge instructions. The P-EDACP tools include PPOs, written discharge instructions with integrated prescription, patient education materials and staff training materials. To address treatment delays noted during A-EDACP implementation, both pathways now include a medical directive to authorize administration of bronchodilators and systemic corticosteroids prior to physician assessment.

CONCLUSIONS: Evidence-based ED pathways for pediatric and adult asthma have been designed to promote best practice in any ED setting. Hospital leads and stakeholder organizations are being engaged to pursue a comprehensive strategy to guide dissemination and implementation support for both pathways.


31 COMMUNITY-BASED EXERCISE PROGRAMS AS A STRATEGY TO MAINTAIN FUNCTION IN CHRONIC DISEASE: A SYSTEMATIC REVIEW

Laura Desveaux\(^1,2\), Marla Beauchamp\(^3\), Dina Brooks\(^2,4\)

\(^1\)Graduate Department of Rehabilitation Science, Faculty of Medicine, University of Toronto; \(^2\)Department of Respiratory Medicine, West Park Healthcare Centre, Toronto, Ontario; \(^3\)Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Harvard University, Boston, Massachusetts, USA; \(^4\)Department of Physical Therapy, Faculty of Medicine, University of Toronto, Toronto, Ontario

RATIONALE: Chronic diseases are the leading cause of death and disability worldwide and account for the majority of healthcare utilization in Canada, affecting more than one half of Canadian adults. Preliminary evidence suggests that community-based delivery models for exercise promote long-term adherence and improve both exercise capacity and health related quality of life in individuals with chronic disease. The primary objective was to describe the structure and delivery of community-based exercise programs designed for chronic disease populations. The secondary objective was to describe the effectiveness of these programs in terms of impact on exercise capacity and health-related quality of life.

METHODS: Randomised trials examining the effects of community-based exercise programs were identified after searching five databases and reference lists of relevant studies in May 2012. Study selection identified articles that included stroke, COPD, arthritis, diabetes, and heart disease—the top five chronic diseases in Canada, as identified by the Public Health Agency of Canada. Two reviewers independently assessed the quality of the studies. The mean difference was utilized for the six-minute walk test (6MWT), while the standard mean difference (SMD) was utilized for all other measures.

RESULTS: Sixteen studies met the inclusion criteria for the primary objective of describing the structure of community-based programs. Twelve studies met the criteria for meta-analysis, representing a total of 1636 individuals with chronic disease. The common effect (WMD) for exercise capacity, evaluated using the 6MWT, was 35.97 (95% CI 15.86-56.08). The SMD for the total score of health-related quality of life measures was 0.35 (95% CI 0.07-0.63).

CONCLUSIONS: Community-based exercise programs have been effectively implemented for multiple chronic disease populations and have similar structures addressing similar underlying impairments. Community-based programs are also superior to standard care with respect to optimizing exercise capacity and health-related quality of life for individuals with chronic disease.

Financial Support: Laura Desveaux is supported by the Ontario Respiratory Care Society, Marla Beauchamp is supported by a CIHR Fellowship, and Dina Brooks is supported by a Canada Research Chair.

32 A QUEBEC KNOWLEDGE TRANSLATION MODEL IN RESPIRATORY DISEASE SURVEILLANCE

Mariève Doucet\(^1,2\), Myriam Gagné\(^3,4\), Valérie Émond\(^1\)

\(^1\)Institut national de santé publique du Québec, Québec; \(^2\)Université Laval, Québec; \(^3\)Institut universitaire de cardiologie et de pneumologie de Québec, Québec

RATIONALE: The respiratory disease (RD) surveillance system of the Institut national de santé publique du Québec aims to collect, analyze, interpret, and disseminate surveillance information. In order to achieve communication for action, the development of a theory-based knowledge translation (KT) model is crucial. Our objective was to develop a theory-based KT...
model in RD surveillance to promote the use of surveillance information in decision-making by policymakers, healthcare providers and researchers.

METHODS: We developed our KT plan following 6 steps: assessing the quality of surveillance information, defining the purpose of communicating information and target audiences, developing messages, and selecting communication channels and ways of marketing information.

RESULTS: Our KT model has been developed to foster the use of surveillance information in decision-making by policymakers, healthcare providers and researchers. The quality of the surveillance information is being assessed on an ongoing basis. A conceptual framework was developed to help identify relevant health indicators used to define the purpose of communication and develop the message. A network of respiratory diseases experts (respirologists, researchers, public health experts, stakeholders and policymakers) plays an advisory and a communication channel role. Tailored résumés of surveillance information are used to market the information for intended audiences.

CONCLUSION: The first stage of the KT model – developing the KT plan for RD surveillance – has been carried out. The aim of the second phase is to implement it whereas a third phase will evaluate its process and outcomes. Our KT model is expected to help decision-making based on surveillance information, and to put forward hypotheses and raise research questions in a purpose to reduce the burden of RD in Quebec.

Financial Support: This project was supported by the Public Health Agency of Canada, the Health Government of Quebec and the INSPIQ.

33 NOT ALL ANTISTATIC VALVED HOLDING CHAMBERS HAVE EQUIVALENT PERFORMANCE: AN EXAMPLE OF WHY EACH VALVED HOLDING CHAMBER (VHC)-INHALER COMBINATION SHOULD BE CONSIDERED UNIQUE

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Medical Aerosol Laboratory, Trudell Medical International, London, Ontario

RATIONALE: The mitigation of electrostatic charge by the use of charge dissipative materials in construction of VHCs is becoming the norm, since the need for a pre-washing step before first use can be avoided altogether.

We report a laboratory-based comparison between two so-called ‘antistatic’ VHCs; Optichamber® Diamond® (OD), Phillips Medical; AC® Girlz®/Boyz® AeroChamber Plus® with Flow-Vu® inspiratory flow indicator (AC), Trudell Medical International) (n=4 devices/group), in which we explored the effect of delayed inhalation, a commonly encountered situation with poorly coordinated patients.

METHODS: An abbreviated Andersen cascade impactor capable of determining fine particle mass <4.7 μm at 28.3 L/min (FPM <4.7μm) was used in conjunction with a proprietary apparatus to simulate 2, 5 and 10 s delay intervals following pressurized metered dose inhaler (Flovent®-125, GSK, plc, 125 μg/actuation fluticasone propionate (FP)) actuation. This approach conforms to current guidance from European regulatory agencies that testing of VHCs should always simulate delayed inhalation. Recovery and assay for FP was undertaken by validated methods involving HPLC+UV spectrophotometry. All values are mean ± SD.

RESULTS: Mass recoveries (131.5±2.9 and 130.7±3.8 μg/actuation for the OD and AC respectively) were close to label claim, validat-

ing system suitability. Values of FPM <4.7μm (μg/actuation) after 2, 5 and 10 s delay were 42.2±3.1; 39.7±1.3; 35.7±2.0 for the AC and 35.0±3.2; 32.7±1.7; 29.3±2.8 for the OD. The ratio FPM<4.7μm-AC/FPM<4.7μm-OD) increased from 1.2 (2 s) to 1.4 (5 s) and to 1.6 (10 s), demonstrating faster depletion of usefulness medicament from the OD.

CONCLUSION: These findings indicate that although a VHC is made from antistatic materials, its ability to retain a therapeutically beneficial portion of the pMDI-delivered dose may vary considerably, and it may not be suitable for the poorly coordinated patient with low tidal volume. Clinicians should be aware that each VHC-pMDI combination should be considered unique.

Financial Support: The authors are employees of Trudell Medical International who funded the study.

34 CLINICAL OUTCOMES FOLLOWING IMPLEMENTATION OF AN EVIDENCE-BASED ORDER SET FOR INPATIENT COPD EXACERBATION MANAGEMENT

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BACKGROUND AND RATIONALE: Gaps between best evidence and actual practice in the inpatient management of COPD exacerbation are well documented. Admission order sets with evidence-based diagnostic and therapeutic options may increase adherence to clinical guidelines, improving quality of care and patient outcomes. We sought to determine the effects of printed and ‘computerized provider order entry’ (CPOE)-based COPD exacerbation order sets on care.

METHODS: We employed a standardized chart review protocol to prospectively review charts of patients admitted for COPD exacerbation at an academic quaternary care hospital in Toronto, Ontario. We recorded process-of-care and patient outcomes, and healthcare utilization before and after order set implementation (January, 2009 – November, 2010).

RESULTS: We identified 201 admissions for COPD exacerbation: 74 in the six-month period preceding order set implementation, and 127 after implementation. In the post-implementation period, 39.4% of admissions made use of the order set. Mean length of stay was 6.5±7.7 days before order sets and 6.3±6.1 days after order sets (p=0.87). Care outcomes that differed significantly between pre- and post periods included: documentation of infection control status, 47/74 (63.5%) versus 127/127 (100%), (p <0.001); assessment by respiratory therapy, 12/74 (16.2%) versus 38/127 (29.9%) (p=0.03); prescription of DVT prophylaxis when indicated, 15/68 (22.1%) versus 68/101 (67.3%), (p<0.001); and prescription of nicotine replacement therapy in smokers, 10/44 (22.7%) versus 24/57 (42.1%), (p=0.04). Other outcomes, including evidence-based ordering of sputum cultures, antibiotics, and BiPAP did not change significantly after order set implementation.

CONCLUSIONS: Evidence-based order sets appear to improve multiple aspects of inpatient COPD exacerbation care. Suboptimal order set uptake in our setting suggests that active implementation is required to ensure usage, and would be expected to drive even greater improvements in care. Larger studies will be required to demonstrate improvements in patient outcomes.

Information on Financial Support: Dr Gupta is supported by the Department of Continuing Education and Professional Development at the University of Toronto.

35 PROVINCIAL IMPLEMENTATION OF AN EMERGENCY DEPARTMENT ASTHMA CARE PATHWAY: LESSONS LEARNED IN KNOWLEDGE TRANSLATION

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BACKGROUND: The Ontario Lung Association’s Adult Emergency Department Asthma Care Pathway for Adults (A-EDACP) is part of the Government of Ontario’s Asthma Plan of Action. The A-EDACP was developed, piloted, revised and disseminated strategically province-wide utilizing key evidence-based knowledge translation (KT) strategies from the Registered Nurses’ Association of Ontario Best Practice Guidelines Toolkit.

PURPOSE: To highlight progress to date, including facilitators and barriers encountered during provincial implementation.

Can Respir J Vol 20 No 3 May/June 2013
Abstracts

METHODS: Local Health Integration Networks (LHNIs) with higher than average return visit rates for adult asthma and hospitals requesting the pathway were targeted. The implementation strategy included stakeholder identification (ED physicians (MDs), registered nurses (RNs), respiratory therapists (RRTs) and administrators) and engagement and environmental readiness assessments. Three-hour workshops were completed in all 12 LHNIs utilizing didactic and interactive methods to introduce the A-EDACP materials and facilitate site-specific implementation approaches. Follow-up surveys were conducted to determine the status of implementation, facilitators and barriers.

RESULTS: 16 workshops were delivered between November 2008 and June 2011 to 373 participants (25 MDs, 154 RNs, 76 RRTs, and 67 administrators) from 159 sites. As of December 2011, 44.1% of hospitals surveyed (n= 93) indicated A-EDACP implementation was either completed (n=22), in progress (n=19) or planned (n=25). Only 11.8% of hospitals indicated no plans to implement and 17.2% hospitals reportedly already following guidelines. Identified barriers included competing priorities (eg Wait Time Strategy) and lack of resources. Facilitating factors included smaller hospital size, simpler approval process and utilization of medical directives.

CONCLUSIONS: Provincial implementation of a validated asthma ED pathway has been challenging, despite using evidence-based KT methodology.

NEXT STEPS: Following a knowledge-to-action cycle, we are addressing identified barriers by engaging key opinion leaders, particularly ED physicians as site champions, further simplifying tools and developing medical directives. Focusing resources, including funding an on-site coordinator, may promote stakeholder engagement and facilitate implementation.

Funding: The Government of Ontario

36

ASBESTOS-RELATED DISEASE IN FORMER WORKERS OF THE ASBESTOS MINE IN BAIE VERTE, NEWFOUNDLAND AND LABRADOR

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RATIONALE: Adverse health effects of exposure to asbestos have been known for more than a century. A causal link has been established between exposure and pulmonary fibrosis, lung cancer, plural mesothelioma, and several other cancers. The purpose of this project was to develop a registry of former workers of the asbestos mine in Baie Verte in order to document their health history and ascertain the number of medically-confirmed cases of asbestos-related disease.

METHODS: Data were collected on 1003 former workers (825 living and 178 deceased) and included information on vital status, employment history at the asbestos mine, medical history, and current health status. The data were collected through questionnaires to former living workers and examination of available medical and employment records for each worker. A job exposure matrix was used to calculate worker cumulative exposure to asbestos.

RESULTS: Based on the records reviewed, medically-confirmed asbestos-related diseases were noted for some workers. Details about the diseases will be elaborated on the poster.

CONCLUSION: The 1003 workers in this project represent less than half of the estimated total number of employees (2,400 to 2,800) of the Baie Verte asbestos operations, which were in existence from the mid-1950s to the mid-1990s. It is possible that workers who were not included in this sample also acquired asbestos-related diseases. Further, as asbestos-related disease can have a latency period of 20 to 40 years from exposure to asbestos to onset of disease, new cases in this sample could very well be diagnosed in the future.

Financial Support: Funded by the Workplace Health, Safety and Compensation Commission of Newfoundland and Labrador

37

THE DEVELOPMENT OF AN OCCUPATIONAL DISEASE REGISTRY OF FORMER WORKERS OF THE ASBESTOS MINE IN BAIE VERTE, NEWFOUNDLAND AND LABRADOR

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RATIONALE: Upper airway obstruction in children with Pierre Robin Sequence can be managed non-surgically, surgically, or in various combinations. Each intervention holds its own advantages and disadvantages. It is a therapeutic challenge to decide which intervention is warranted and the optimal timing to proceed. This population-based retrospective analysis examined factors that led to the decision to perform a particular intervention, as well as outcomes.

METHODS: A chart review was done on patients with Pierre Robin Sequence seen at two children’s hospitals in Alberta between 2000 and 2010. Prevalence of non-surgical (nasopharyngeal intubation, CPAP), and surgical (glossoxy, mandibular distraction, tracheostomy) interventions, as well as no intervention, was examined. Comparisons were made of factors and outcomes such as gender, gestational age, birth weight, associated syndromes, feeding method, time to intervention, length of admission, polysomnogram results, and mortality rate. Analyses included ANOVA and Pearson Chi-Square tests.

Financial Support: Funded by the Workplace Health, Safety and Compensation Commission of Newfoundland and Labrador

Pediatric / Pédiatrie

38

SURGICAL VERSUS NON-SURGICAL INTERVENTIONS TO RELIEVE UPPER AIRWAY OBSTRUCTION IN CHILDREN WITH PIERRE ROBIN SEQUENCE

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1 University of Calgary, Alberta Children’s Hospital; 2 University of Calgary, Calgary; 3 University of Alberta, Stollery Children’s Hospital, Edmonton, Alberta

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Financial Support: Funded by the Workplace Health, Safety and Compensation Commission of Newfoundland and Labrador

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RESULTS: Out of 139 charts identified, 64 (46%) patients did not receive an intervention. Interventions included nasopharyngeal intubation (n=28, 20.1%), CPAP (n=20, 14.4%), glossectomy (n=15, 32.4%), mandibular distraction (n=5, 3.6%), and tracheostomy (n=19, 13.7%). More females than males received a nasopharyngeal tube (19 versus 9, p=0.02). Patients with an associated syndrome were more likely to receive a tracheostomy than those with an isolated presentation (p<0.05). Children who received a tracheostomy also had significantly lower birth weights (mean 2714g versus 3114g, p=0.03), longer hospital admissions (p<0.001), and a higher complication rate at 3 years (p<0.01). There were no significant findings between the other interventions and variables.

CONCLUSION: Nasopharyngeal intubation and glossectomy were most frequently performed, although almost half of patients did not require any intervention. Apart from tracheostomy, there were no risk factors or outcomes to suggest which other intervention is optimal. Decisions made between healthcare providers and patient provider seemed to be on a case-by-case basis.

39
STUDIES OF SLEEP DISTURBANCE IN FAMILY CAREGIVERS OF TECHNOLOGY DEPENDENT CHILDREN
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RATIONAL: The number of technology dependent children (TDC) including those on long-term ventilation is on the rise. Society relies on family caregivers of TDC to provide highly skilled and vigilant care in their homes 24-hours per day. This extraordinary responsibility has been linked to chronic sleep disturbance that places family caregivers at risk of negative heath and related outcomes.

METHODS: Sleep in family caregivers of TDC was the focus of a systematic review of the literature. All relevant databases were searched for the terms: caregiver*, carer*, parent*, mother*, father*, grandparent* AND sleep*, sleep deprivation*. 

MAIN RESULTS: Over 1,200 study abstracts were retrieved and eight studies met criteria for inclusion. The studies were highly varied with respect to methods, measures, thereby precluding a metasynthesis, thus the results of this review are presented as a narrative.

SIGNIFICANT RESULTS: Reports of sleep disturbances were highly variable (51% to 100%). Studies using subjective sleep measures reported that family caregivers of TDC get less than 6 hours of sleep per night and one full hour less than family caregivers of children with cystic fibrosis and/or healthy children. Very poor sleep quality has also been self-reported. These findings, together with qualitative and other subjective accounts suggest that family caregivers of TDC experience significant sleep restriction, poor sleep quality, and are at risk for negative consequences of chronic sleep deprivation.

CONCLUSION: This review determined that sleep disturbance in family caregivers has been investigated using only subjective measures. This review also pointed towards the influence of multiple factors (i.e. caregiver, child and environmental) on sleep disturbance in family caregivers of TDC. Results of these studies are to be interpreted with caution however, given the lack of objective data, thus signaling the need for further investigation of sleep disturbance and related outcomes in family caregivers of TDC.

40
RSV HOSPITALIZATION IN CYSTIC FIBROSIS IN THE CANADIAN REGISTRY OF SYNAGIS® (CARESS) FOLLOWING PROPHYLAXIS (2005-2012)
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BACKGROUND/AIMS: Aboriginal infants have substantially higher risks for respiratory illness (RI) and respiratory syncytial virus (RSV) hospitalizations compared to non-Aboriginal infants. The purpose of the present study was to compare hospitalization rates for RI events and RSV infection in Aboriginal versus non-Aboriginal infants in the CARESS database.

METHODS: A prospective, observational registry of infants from 32 Canadian sites who received ≥1 dose of palivizumab during the 2005-2012 RSV seasons was compiled. Utilization and hospitalization outcomes were collected monthly throughout respective RSV seasons.

RESULTS: 13,315 infants were recruited (450 Aboriginal; 12,865 non-Aboriginal). A greater proportion of Aboriginal infants had siblings (81.6% versus 62.9%, p<0.005), were exposed to smoking (69.8% versus 25.1%, p<0.0005) and had ≥5 individuals in the household (61.8% versus 25.5%, p<0.0005) and a lower proportion were a multiple birth (19.6% versus 29.0%, p<0.0005). Aboriginal infants were less compliant with prophylaxis whether calculated by injection intervals (66.7% versus 73.5%, p=0.001) or expected number of injections (50.4% versus 66.6%, p=0.0005) during the season. Aboriginal infants had significantly higher RSI (11.8% versus 6.4%, p<0.0005) and RSV hospitalization (2.9% versus 1.5%, p=0.048) rates. A Cox proportional hazards analysis in Aboriginal infants found the risk of RSV-positive hospitalization was higher among non-compliant than compliant infants (hazard ratio=4.0, 95%CI 1.1-15.1, p=0.040). 

CONCLUSIONS: This study confirms that several demographic and environmental factors that are prominent in increasing risk of both RSV hospitalizations in high-risk infants including 239 with cystic fibrosis (CF). This study compares respiratory illness (RI) and RSV positive hospitalization (RSVH) rates in CF infants versus: 1) those with other underlying medical disorders (MD) and 2) those who meet standard indications for RSV prophylaxis (SD) in the database.

METHODS: A prospective, observational registry of infants from 32 sites who received ≥1 dose of palivizumab during the 2005-2012 RSV seasons. Palivizumab utilization and RI outcomes were collected monthly over each individual season.

RESULTS: 13,315 infants were enrolled (CF: 239, 1.8%; MD: 1863, 14.0%; SD: 11213, 84.2%). There were significant differences (p<0.05) between the three groups in gestational age, birth weight, and in the proportions of: males, Caucasians, siblings, multiple births, daycare attendance (both parents and their siblings), smokers in the household, >5 people in the household, and immediate family history of atopy, and complexity of neonatal course (with the exception in proportions of incidence necrotizing enterocolitis during neonatal course). Infants with CF had a significantly lower hospitalization rate (3.8%) than MD (11.2%, p<0.0005) but not SD (5.9%, p=0.207). In terms of RSV-positive hospitalizations, there was no significant difference between CF and MD (0.54% versus 2.22%, p=1.000) or SD (1.48%, p=0.232). In the Cox proportional analysis, hazard ratios of time to first RSVH in CF were similar to SD (Exp(B) = 0.354, 95%CI = 0.049-2.531, p=0.301) and MD (Exp(B) = 0.268, 95%CI = 0.037-1.968, p=0.196).

CONCLUSIONS: This is the largest report of CF infants who have received palivizumab world-wide. Despite RI rate differences, RSVH rates appear similar to those in MD and SD.

Financial Support: Dr Paes, Dr. Mitchell, and Dr. Lanctôt have received investigator-initiated research funding from Abbott Laboratories Limited and have been compensated as advisors and/or lecturers for Abbott and MedImmune. Dr Mitchell has received research grants from MedImmune, SIDS Calgary, Alberta Centre for Child, Family & Community Research, and Alberta Law Foundation. Miss Li has received a speaker’s honorarium from Abbott.
infection and overall RI hospitalizations are at play in Aboriginal infants. Improving compliance with prophylaxis may reduce RSV hospitalization rates in this vulnerable population.

42

A COMPARISON OF QUALITY OF LIFE (QOL) PERCEPTIONS: CHILDREN WITH ASTHMA AND THEIR CAREGIVERS
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BACKGROUND: Asthma exacerbations are a leading cause of school absenteeism and time lost from work, affecting the QOL of children with asthma and their caregivers. There is limited understanding of asthma related QOL for rural families.

OBJECTIVE: The objective of this study is to determine the relationship between three QOL scales administered to children with asthma and their caregivers living in rural Saskatchewan.

METHODS: Data for this research was previously collected in 2005-2007 for the rural population-based case-control study of asthma in children. Children, ages 6-18 years, with physician-diagnosed asthma (n=75) were selected for this analysis. During a clinic visit, children with asthma completed the Pediatric Asthma QOL Questionnaire (PAQLQ), parents completed the Child Health Questionnaire (CHQ-PF50) and the Pediatric Asthma Caregiver QOL Questionnaire (PACQLQ). QOL scores were measured using the mean scores with higher scores indicating better QOL.

RESULTS: Children with asthma had the lowest scores on the Activity Domain (PAQLQ), indicating children's QOL was largely influenced by limitations to their activity. Parents lowest score was for sleepless nights on the Emotional Domain (PACQLQ), indicating children's QOL was largely influenced by visceral and subcutaneous fat area from a single abdominal cross-sectional image at the level of the third lumbar vertebra.

RESULTS: Thoraco-abdominal CT-scan of 60 patients (27 males/33 females, mean age of 65 ±10 years and body mass index of 15±5 Kg/m²) with advanced lung cancer of stage 4 (n=40) and 3 (n= 20) were analysed. The average area of muscle, visceral fat and subcutaneous fat were 142±115 cm², 131±66 cm² and 128±28 cm² respectively. Finally, 42% of patients had a lumbar muscle index suggesting cachexia (≤55 cm²/m² for men; ≤39 cm²/m² for women).

CONCLUSION: At diagnosis, a large proportion of patients with advanced lung cancer presented a cachectic state.

Financial Support: Fondation J.D Bégin

44

RISK FACTORS FOR POSTOPERATIVE RECURRENCE OF PRIMARY SPONTANEOUS PNEUMOTHORAX, WITH AN EMPHASIS ON CANNABIS CONSUMPTION
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RATIONALE: Little is known about risk factors unrelated to surgical technique that may increase postoperative recurrence rates in patients with primary spontaneous pneumothorax. These may include tobacco smoking, although available data are extremely limited. Albeit sometimes implicated in the pathogenesis of spontaneous pneumothorax, the role of cannabis as a risk factor for recurrence in the postoperative setting is largely unknown.

OBJECTIVE: Evaluate risk factors for postoperative recurrence in patients undergoing surgical treatment of primary spontaneous pneumothorax.

METHODS: We conducted a retrospective review of patients admitted for surgical treatment of primary spontaneous pneumothorax between 1995 and 2011. Patient files were reviewed for clinical, radiological, and pathological data, as well as tobacco, cannabis and other drug use. Patients over 40 and/or with known COPD were excluded.

RESULTS: 133 patients were available for review. Ninety patients met the inclusion criteria for the study. 60 patients were male and 30 female. Average age at the first episode of pneumothorax was 24 years (±6,83). 54% of patients were tobacco smokers and 32,7% reported regular cannabis use, which exceeded rates for the Canadian adult population in 2011 (9,1% according to Statistics Canada). 10 patients (11,1%) had a postoperative recurrence of pneumothorax. Cannabis use was associated with an increased recurrence rate, with an odds ratio of 4,23 95% CI (0,88 – 20,3). The presence of bullae in the resected specimen was associated with a trend towards a decreased risk, with an odds ratio of 0,203 95% CI (0,038 – 1,08). Interestingly, tobacco smoking was associated with a significantly decreased risk of postoperative recurrence, with an odds ratio of 0,136 95% CI (0,03 – 0,67). Sex and side of surgical intervention did not affect outcomes.

CONCLUSION: Cannabis use increased the risk of postoperative recurrence in patients with spontaneous pneumothorax. Interestingly, tobacco smoking was associated with a decreased risk of recurrence.

43

BODY COMPOSITION ANALYSIS FOR PATIENT WITH LUNG CANCER USING COMPUTED TOMOGRAPHY IMAGE ANALYSIS
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RATIONALE: With 1.6 million new cases diagnosed each year and 1.3 million deaths, lung cancer is the leading cancer-related death worldwide and it represents a pressing health issue. Patients with lung cancer are more likely to experience cachexia, a severe debilitating disorder causing fatigue, weight loss, muscle wasting and associated with reduced physical function, increased chemotherapy toxicity and reduced survival. This syndrome occurring in about 80% of advanced cancer patients is the direct cause of death in about 20% of cases. However, despite the importance of cachexia in lung cancer, it has been mainly studied from several assessment methods which do not usually differentiate muscle from other tissues.

AIM: To analyze body composition of patients with lung cancer at diagnosis using computed tomography (CT-Scan) image analysis.

METHODS: This is a retrospective study extending over a period of 3 years conducted at the Institut universitaire de cardiologie et de pneumologie de Quebec (2009-2012). We listed patients newly diagnosed with lung cancer who had a thoraco-abdominal CT-scan performed in our institution. Following the collection of clinical data from patient records, we used SliceOmatic software to quantify muscle area, visceral fat area and subcutaneous fat area from a single abdominal cross-sectional image at the level of the third lumbar vertebra.

RESULTS: Thoraco-abdominal CT-scan of 60 patients (27 males/33 females, mean age of 65 ±10 years and body mass index of 15±5 Kg/m²) with advanced lung cancer of stage 4 (n=40) and 3 (n= 20) were analysed. The average area of muscle, visceral fat and subcutaneous fat were 142±115 cm², 131±66 cm² and 128±28 cm² respectively. Finally, 42% of patients had a lumbar muscle index suggesting cachexia (≤55 cm²/m² for men; ≤39 cm²/m² for women).

CONCLUSION: At diagnosis, a large proportion of patients with advanced lung cancer presented a cachectic state.

Financial Support: Fondation J.D Bégin
45
diagnostic yield of flexible bronchoscopy without guidance (aspiration, brushing, bronchoalveolar lavage) for peripheral pulmonary neoplasia

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BACKGROUND: The diagnostic yield of non-guided bronchoscopy in the investigation of peripheral pulmonary lesions remains largely unknown. A global sensitivity of 78% (57% for transbronchial biopsy, 54% for brushing, 43% for bronchoalveolar lavage) has been reported in the literature. However, these studies used fluoroscopic guidance and included endobronchial lesions.

OBJECTIVES: To assess the sensitivity of flexible bronchoscopy (aspiration, brushing and bronchoalveolar lavage) without fluoroscopic/ultrasound guidance for the diagnosis of peripheral pulmonary lesions and to establish clinical and radiological characteristics associated with increased sensitivity.

METHOD: Retrospective study of consecutive patients (n=213) with a final diagnosis of peripheral (no endobronchial lesion) cancer who underwent bronchoscopy with aspiration, brushing and bronchoalveolar lavage at the IUCPQ between April 2008 and December 2010.

RESULTS: Global sensitivity of bronchoscopy was 25.8% (14.2% for aspiration, 18.8% for brushing and 12.2% for cytologic bronchoalveolar lavage). Non-guided brushing was the technique that added the most to the exam sensitivity as it was the only positive sample in 6.6% of cases, as opposed to 3.3% and 2.8% for aspiration and lavage, respectively. Techniques’ sensitivity was influenced by patient’s age, bronchoscopist (respirologist vs. fellow), size of the lesion, cancer stage, PET scan SUV, distance from the hilum, presence of a bronchus sign and cancer histology.

CONCLUSIONS: The global sensitivity of bronchoscopy without guidance for peripheral pulmonary lesions was 25.8%. Among the studied techniques, brushing appeared to be the most sensitive. Various clinical and radiological characteristics impacted the probability of obtaining a diagnosis by bronchoscopy and hence, the relevance of sampling.

46
functional outcomes pre- and early post-lung transplantation

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RATIONALE: There has been limited research examining functional changes in a cohort of individuals pre- and early post-lung transplantation.

METHODS: Peripheral muscle strength (isometric quadriceps torque (QFT), functional exercise capacity (6-minute walk distance (6MWD)), health-related quality of life (HRQOL) (SF-36 and St. George’s Respiratory Questionnaire (SGRQ)) and physical activity (daily steps and time spent during Submaximal exercise in Pulmonary Arterial Hypertension)

Can Respir J Vol 20 No 3 May/June 2013
Abstracts

49 OSTEOPONTIN LUNG EXPRESSION IS A MARKER OF DISEASE SEVERITY IN PULMONARY ARTERIAL HYPERTENSION

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RATIONALE: Proliferation of smooth muscle cells (SMCs) and pulmonary arterial remodelling are key mechanisms in the pathogenesis of pulmonary arterial hypertension (PAH). Osteopontin (OPN) is a pleiotropic cytokine involved in the proliferation of pulmonary vascular smooth muscle cells (PASMCs). We recently discovered that OPN is upregulated in the lungs of patients with PAH associated with pulmonary fibrosis, suggesting that the lung tissue is a source of OPN. We hypothesized that OPN lung expression is elevated in PAH and is correlated with hemodynamics.

METHODS: Microarray analysis (Affymetrix®) was performed after RNA was extracted from explanted lungs in 15 patients with PAH (mPAP 2.13, age 41±12 years, 6 idiopathic PAH, 4 connective tissue disease, 4 congenital heart disease and 1 chronic thromboembolic PAH) who underwent lung transplantation (LTx) and 11 normal controls (normal lung tissue surrounding lung cancer resections). Pulmonary artery pressures (PAPs) were measured non-invasively (Nexfin HD, BMEYE, Amsterdam, The Netherlands) at the end of exercise (10.7±2.9 vs 9.8±2.1 L/min, p=0.47). Arterial O2 desaturation during exercise was more pronounced for PAH patients (5.5±5.1 vs. 0.0±5.9 %, p=0.01). However, O2 supplementation did not modify muscle [HHb] during exercise (p=0.66). Changes in [HHb] during submaximal exercise correlated with exercise capacity (R²=0.37, p<0.01).

CONCLUSION: These preliminary results suggest that PAH patients exhibit an inadequate muscle O2 supply during submaximal exercise that is not related to cardiac output or arterial O2 saturation. Impaired O2 delivery may contribute to exercise intolerance of PAH subjects.

Financial Support: This work was supported in part by the CIUQPCQ graduate student grant and by Laval University School of Medicine graduate grant to S. Malenfant.
In vivo, local intramuscular injection of miR-126 antagonist within the quadriceps, significantly reduced exercise tolerance compared to rats injected with transfection control. Finally, miR-126 expression in the patients serum was downregulated and correlated with VO2\text{peak}. CONCLUSION: We demonstrated for the first time that exercise intolerance in PAH is associated with the decrease of skeletal muscle angiogenesis secondary to the downregulation of miR-126.

Financing: This study has been funded by the IRSC.

52

PIM-1: A NEW BIOMARKER IN PULMONARY ARTERIAL HYPERTENSION

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BACKGROUND: Provirus Integration site for Moloney murine leukemia virus (Pim-1) is an oncoprotein overexpressed in lungs from pulmonary arterial hypertension (PAH) patients and involved in cell proliferation via the activation of the NFAT/STAT3 signaling pathway. Pim-1 could be a potential new biomarker specific of pulmonary vascular remodelling in PAH.

HYPOTHESIS: We hypothesized that: 1) Pim-1 plasma levels measured by ELISA would discriminate patients with heritable/idiopathic PAH from controls; 2) vasoactive/immune PAH (VR-PAH) presumably characterized by less pulmonary vascular remodeling would exhibit lower Pim-1 plasma levels; 3) among PAH patients, Pim-1 plasma levels would correlate with PAH severity.

METHODS: Pim-1 plasma levels were measured by ELISA (Human Pim-1: ELISA Kit, Cusabio Biotech Co., Ltd) at the time of catheterization in 49 PAH patients, including IPAH (n=19), VR-IPAH (n=5) CTD-PAH (n=16) and PAH related to congenital heart disease (n=9). Fifty controls were also recruited. The capacity of Pim-1 to discriminate PAH from controls and its association with disease severity were assessed.

RESULTS: Pim-1 plasma levels were higher in PAH than in controls (9.2±4.0 vs 7.2±2.4 ng/ml, p<0.01). Pim-1 was elevated in idiopathic PAH and in CTD-PAH, whereas normal values were observed in PAH-VR and PAH-CHD. Pim-1 appropriately discriminated proliferative PAH from controls (AUC 0.91 using ROC curve). Amongst PAH patients, Pim-1 correlated with traditional markers of PAH severity. The 1-year survival was 97% and 47% for PAH patient with baseline Pim-1 levels lower and higher than 11.1 ng/ml, respectively (HR 11.4[3.3-39.7]; p<0.01). Adjustment for hemodynamic and biochemical variables, Pim-1 levels remained an independent predictor of mortality (p<0.01).

CONCLUSION: The oncoprotein Pim-1 serum levels were elevated in patients with PAH. Amongst PAH patients, Pim-1 levels correlated with disease severity and predicted outcomes. Pim-1 is thus a promising new biomarker in PAH potentially related to the active pulmonary vascular remodeling in PAH.

Information sur le financement: SP is clinician-scientist of the FRSQ. SB holds a Canadian Research Chair and a Canadian Research Chair on Vascular Pathologies at Université Laval. Sébastien Renard has received a fellowship grant from the Fédération Française de Cardiologie, Actelion Pharmaceuticals France and Assistance Publique des Hôpitaux de Marseille.

53

TWO CASES OF PSEUDOHYPOALDOSTERONISM TYPE 1 WITH NOVEL GENETIC MUTATIONS: LIFE-THREATENING NEONATAL SALT WASTING AND HYPERKALEMIA WITH A POSITIVE SWEAT TEST AND CF-LIKE ILLNESS

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INTRODUCTION: Autosomal recessive Pseudohypaldosteronism type 1 (PHA1) is a rare disorder of mineralocorticoid resistance. It is due to defects in the epithelial sodium channel (ENaC), which is found in the kidneys, airways and sweat glands. It presents with renal salt wasting in the neonatal period. The diagnosis is relevant to pulmonologists as it is also associated with a high sweat chloride and phenotypically mimics the early lung manifestations of CF.

CASES: We present a series of 2 female infants with PHA1 who developed severe laryngitis, vomiting and dehydration in the first week of life. They both had serum potassium >10 mmol/L, complicated by ventricular tachycardia, sodium <130 mmol/L, acidosis and high plasma aldosterone. Sweat chloride levels were 146 mmol/L and 155 mmol/L. Both infants developed right upper lobe pneumonia within the first 4 months of life. They are being managed in the CF clinic with frequent cough swab surveillance and early antibiotic treatment, regular physiotherapy, sodium polystyrene and sodium chloride supplements. By 15 months and 4 months of age, neither child has developed any further respiratory complications. Both cases have different novel mutations in the SCNN1A gene, resulting in premature stop codons. These mutations are predicted to be deleterious for the 61 subunit of ENaC.

DISCUSSION: PHA1 is associated with increased airway surface liquid and mucociliary clearance, likely secondary to the effect of the ENaC’s role in regulating sodium content of airway fluid. Detailed ciliary function in this patient group is unknown. We are currently undertaking ciliary beat frequency and beat pattern analysis in these 2 cases to precisely determine ciliary function in PHA1.

54

TRENDS IN CANADIAN RESPIRATORY CLINICAL TRIALS FROM 2001-2011

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RATIONALE: Respiratory diseases affect over 3 million Canadians and are the third most common reason for hospitalization and death.1 Clinical research facilitates patients’ access to innovative medicines, increases knowledge acquisition by clinicians, and has a potential impact on the clinical economy and the healthcare system.2 While there are currently more than 3000 clinical trials ongoing in Canada, the number of trials conducted in respiratory is unknown. The objective of this study was to determine the trends of respiratory clinical trials in Canada from 2001-2011.

METHODS: We searched Trialtrove®, 2012 (Citeline, an Informa UK business), a database containing summarized clinical trial information, for trials conducted in Canada between 2001-2011 in the following therapeutic areas: allergic rhinitis, asthma, chronic obstructive pulmonary disease, cystic fibrosis, respiratory infections, pulmonary fibrosis and smoking cessation.

RESULTS: From 2001-2011, in total, 82 trials were performed in allergic rhinitis, 140 in asthma, 110 in chronic obstructive pulmonary disease, 40 in cystic fibrosis, 137 in respiratory infections, 12 in pulmonary fibrosis and 40 in smoking cessation. The total number of trials conducted in Canada within the respiratory therapy area increased from 2001 and peaked in 2007 with 73 trials conducted in Canada this year. Of the trials performed during this 10 year period, 37 were phase I, 165 were phase II, 215 were phase III and 119 were phase IV trials. The majority of trials were industry sponsored.

CONCLUSIONS: Over the past 10 years, the number of clinical trials within the respiratory therapeutic area conducted in Canada has actually increased, solidifying Canada’s leadership role in respiratory research.
55 PERIPHERAL SKELETAL MUSCLE: CHARACTERIZATION OF ITS REGENERATIVE POTENTIAL IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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RATIONALITY: Chronic Obstructive Pulmonary Disease (COPD) is often associated with limb muscle atrophy, which decreases quality of life and functional capacity in affected individuals. Impaired satellite cells activation, proliferation and differentiation affecting skeletal muscle regeneration could contribute to the progression of muscle atrophy in patients with COPD.

METHODS: Biopsies of the vastus lateralis were obtained from patients with COPD (mid-thigh muscle cross-sectional area (MTCSA) > 70 cm², n=11; MTCSA<70 cm², n=6) and from healthy subjects (n=7). Accumulation of Notch and Wnt related-proteins were quantified using whole muscle extracts. Satellite cell number and muscle regenerative events were counted on cryosections using nuclear immunostaining. Primary muscle cell cultures were performed from muscle biopsy specimens to measure satellite cell proliferation rates and to assess commitment to differentiation.

RESULTS: The switch between Notch (proliferation) and Wnt (differentiation) signaling pathway appears to be dysfunctional leading to a pro-proliferative state suggested by the increased expression of MyoD, Myf5, GSKa/b and phospho-Numb in patients with COPD (MTCSA <70 cm²). Satellite cell numbers were similar between groups. The number of central nuclei per 100 fibers was increased in patients with COPD (MTCSA >70 cm²) compared to patients with COPD (MTCSA<70 cm²) and controls. In COPD, a decreased in the proliferation of satellite cells was initially observed in vitro at 48 hours while their number was increased at 96 hours compared to controls. During myogenesis, an altered pattern of MRFs (Pax7, Myf5 and Myogenin) accumulation was observed between patient with COPD and patient with normal lung function. Finally, accumulation of the myosin heavy chain protein was reduced during myogenesis.

CONCLUSIONS: Based on these results, the transition between the Notch and the Wnt pathway seems to be defective maintaining satellite cells into a proliferative state. Deficiencies in their activation and their myogenic program could contribute to the maintenance or the development of muscle atrophy in this population.

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*These authors contribute equally to this study


56 THE CANADIAN RESPIRATORY JOURNAL – ONE YEAR ON AND STILL IMPROVING!

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BACKGROUND: Since 1994 when the Canadian Respiratory Journal (CRJ) was introduced, it has become the premier Canadian journal for the dissemination of respiratory and pulmonary research and clinical practices. In 2010, it was ranked 26th worldwide in the category of Pulmonary and Respiratory Medicine (ScImago Journal Rank). It is the official Journal of the Canadian Thoracic Society (CTS) and the Canadian Critical Care Society (CCCS). The CRJ began an online-only submission system in May 2011, when the new Editor-in-Chief, Dr Peter Paré, also began his tenure. Since then, many changes have been instituted.

A new format for case reports, the Clinico-Pathological Conference (CPC) series has been implemented and now focuses on learning/teaching. Discussion is still underway with regard to an online format for awarding CME credits for readers of this series.

During the past year, several new features have been introduced, including a Focused Review feature and an Images in Respiratory Medicine feature, both of which we hope will appeal to our readership.

FUTURE DIRECTIONS:

• Ongoing discussions to formalize a relationship with the Canadian Sleep Society (CSS).

• CRJ is committed to the translation of knowledge and, to this end, intends to publish a Knowledge Translation issue with solicited articles from top researchers in the field.

• More themed issues are planned similar to the Aboriginal Health issue published in the CRJ Nov/Dec 2012.

Support: The Canadian Respiratory Journal and Canadian Thoracic Society
AUTHOR INDEX

A
Abdelhadeed T .................. 34
Abalhadi T .................. 23
Ali Alwan L .................. 1,3
Ali R .................. 33
Athon S .................. 30,35
Audrey C .................. 2
Audusseau S ................. 3
Avvakoumovna V ............ 33

B
Babayan A .......... 29
Bacon SL ........... 21
Baglole CJ .................. 1,3
Bailey P ............. 16
Bakal D .................. 8
Barrier M .................. 5
Beaucage F .................. 21
Beauchamp G ............... 43
Beauchamp M ............... 31
Beauchamp MK .................. 18
Bendavid Y ............... 27
Bérubé J-C .................. 7
Bisserier M .................. 4
Bonnet S .............. 5,48,50,51,52
Bordeau M ............... 47
Bornestein S .............. 36,37
Bous Y .................. 4,7
Boolet L-P ............... 7,47
Bowdish DME .............. 6
Breulls-Bonnet S ........... 5,51,52
Brooks D ........... 18,19,31,46
Bryce R .................. 10
Butcher S .................. 17
Butt A ............... 36,37

C
Cafaro J .............. 26
Camp PG ........... 13,14
Canadian Chronic Disease
Surveillance System Chronic
Respiratory Disease Working
Group .................. 13
Caroline L .................. 2
Chambers-Evans J .... 20
Chang Y .................. 1,3
Châtel-Thim E .............. 15,21
Chilvers M .................. 53
Choong K .................. 25
Claveau C .................. 24
Cloutier JD ............... 16
Counts V .................. 43
Court chene A .............. 5
Couture C ............... 4,45,51
Crater G .................. 54

D
D’Souza L ............... 19
Dauncey L ............... 8
Davidson W .............. 8
de Lorimier M ............. 21
de Perrot M .............. 49
D’Eubigier R .............. 50,55
Delage A ............... 45
Dell S .................. 12,22
Demers P .................. 36,37
Denis R .................. 11
Desveaux L .............. 31
Dicks E ............... 36,37

Domani J .................. 10
Doucet M ............... 13,32
Drapeau C .................. 45
Dubé A .................. 50
Ducharme FM ............... 30
Duclos C .................. 15
Ducul E ............... 8
Dumont M .................. 15

E
Edelman DH ............... 1,3
Émond V .................. 32
Eve T .................. 2

F
Farrell G ............... 36,37
Feldman L .............. 12,22
Ferrone M ............... 26
Foty R .................. 22
Fowler K .................. 36,37
Fox G .................. 36,37

G
Gagné M .................. 32
Garvey NJ .................. 13
Gaudreau N .................. 7
Gauthier E .................. 20
Gershon AS ............... 12,13,22
Gilbert CP ............... 13
Goldstein R ............... 19
Goldstein RS .............. 18
Goodridge D ............... 17,42
Granton JT .................. 49
Guez M .................. 24
Gupta S .................. 34

H
Hagel L .................. 10
Hakayo A .................. 1
Hamid Q .................. 1,3
Harkness H ............... 33
Hathorn IC ............... 53
Helm D .................. 46
Hercun J .................. 44
Horvey KJ ............... 17

J
Jabbour M .................. 35
Jabbour M .................. 30
Janaudis-Ferreira T ........... 18,19
Jérémén-L ............... 2
Johnson JR ............... 3
Jouabt JR .................. 20

K
Kam K .................. 38
Kaminsia M ............... 23
Karunamayake C .............. 10
Keilthy K .................. 39
Keshavjee S ............... 14
Kirkham A .................. 14
Kiryuchuk S ............... 10
Kitchlu A .................. 34
Koo KKY .................. 25
Koziskyj A .................. 13

L
L’Archevêque J ........... 28
Labbé C ............... 45
Labrecque M ............... 11
Labrecque M ............... 28

Lacasse Y .............. 43
Lalancette J-S .............. 43
Lamontagne M .............. 4
Lancôt KL ............... 40,41
Larsen T .................. 25
Lavigne AS ............... 26,29
Lavoielette M .............. 4
Lavrie KL ............... 21
Lavrie-Charland E ........... 7
Lawson J .................. 10,42
Lemire BB .................. 55
Li A .................. 40,41
Liscikai C ............... 22,26
Loughhead MD ............. 12,26,30,35
Lucy D .................. 25

M
MacLean J ............... 38
Madeley C ............... 26,35
Maigny V .................. 48
Malenfant S ............... 48,51
Malkin B .................. 2
Malraux B ............... 34,48,50,55
Marcinuk D ............... 13
Maria-Helena J .............. 2
Marie-Claude R .............. 2
Marjorie B .................. 27
Marquis P .................. 27
Martz S .................. 45
Martin JG .................. 1
Martin S .................. 35
Mathilde C .................. 2
Mathur S .................. 46
McKay M .................. 38
McMillan Boyles G .............. 16
MeaR L .................. 13
Meliche J ............... 5
Mesbah A ............... 27
Milos A .................. 28
Mitchell I .................. 38,40,41
Mitchell JP .................. 33
Montgomery P ............... 16
Morissette MC .............. 6
Moulic G .................. 15
Mura N .................. 49
Murphy TG .................. 36,37

N
Nagel MW .................. 33
Neis B .................. 36,37
Neyron A-S .................. 48
Nicholls B .................. 54

O
Olajos-Clow J ............... 30,35
Oddy J .................. 36
Ouellette D .................. 44

P
Paes BA .................. 40,41
Pahwa P .................. 10
Paquet J .................. 15
Paré M-E ............... 55
Paré P .................. 56
Parenteau S ............... 21
Paulin R .................. 52
Pepin V .................. 15,21
Pilbout P ............... 52
Portier A .................. 50
Potus F .................. 48,51
Prosser R .................. 13
Provencher S ............... 5,45,48,51,52

R
Rakovich G ............... 24,27,44
Reimer KC .................. 13
Renard S .................. 52
Rennie D .................. 42
Rennie DC .................. 10
Rik AK .................. 15,21
Robles PG .................. 18

S
Saeid D .................. 43,48
Saskatchewan Rural Health
Study (SRHS) Research Group
10
Sayegh-Smith J .............. 11
Schneider H .................. 33
Schreiner R .................. 8
Schwartz R .................. 29
Seaton C .................. 53
Sébastien B .................. 2
Senn P .................. 6
Sim C .................. 14
Simard S .................. 52
Simatojo J .................. 12,22
Singh LG ............... 46,49
Strois C .................. 27
Small S .................. 35
Sokoluk S .................. 42
Spier S .................. 38
Stampfl MR .............. 6
Stanojevic S ............... 12,22
Steeve P .................. 2
Stremel R .................. 39
Su Z .................. 54

T
Tacon CE .................. 54
Tait A .................. 26
Take T .................. 36,37
Tardif M ............... 24
Thain K .................. 56
The Merck-Laval-UBC
Groningen Lung eQTL
consortium .............. 4
Thériault M-E ............... 55
To T .................. 12,13,22,26
Tremblay E .................. 5
Tremblay M-P .............. 5
Troini R .................. 23
Tullis E .................. 34
Turnel J .................. 47

V
Vanderloo S ............... 13
Véronique T ............... 2

W
Wardini R ............... 21
Wickerson L .............. 46
Wittmans M ............... 38

Y
Yeung M .................. 26
Yun Z .................. 49

Z
Zarins S .................. 29
Zhao Y .................. 49
Zheng B .................. 11
Zheng H .................. 12
Zhu J .................. 12,22
Zielinski D ............... 23