THE 2009 COPD CONFERENCE

Reactive Past, Preventive Future

Vancouver, British Columbia
In early February 2009, around 30 internationally recognized Chronic Obstructive Pulmonary Disease (COPD) researchers and clinicians gathered in Vancouver to share their thoughts and expert knowledge on COPD... from its pathogenesis and treatment, to devising a new “blueprint” for COPD research for the next generation.

The conference consisted of a public forum, two full days of presentations, and a celebration dinner for Dr. James Hogg, the founder of the pulmonary research group at St. Paul’s Hospital and inspiration behind this event.

Over the course of the conference, long-time friendships were renewed, and new connections made. The collaborative nature of the event shone through in the camaraderie and humour shared by speakers and participants during breaks and lunches, while the cutting-edge research being presented by speakers (much of it so new it had not yet been published) spoke to the high calibre of the event.

Such an impressive spectrum of leaders in lung health and disease all gathered together at the conference reflects the enormous regard that investigators, educators, and the international community has for the COPD research being carried out in British Columbia for more than three decades. This local excellence is synonymous with Dr. James Hogg.

The World Health Organization (WHO) estimates 80 million people have moderate to severe chronic obstructive pulmonary disease, which will be the third-leading cause of death worldwide by 2030. Total deaths from COPD are projected to increase by more than 30% in the next 10 years unless urgent action is taken to reduce the underlying risk factors, particularly tobacco use. It is estimated that half of those suffering from COPD are undiagnosed, leading to increased burden, suffering and costs.

The report that follows aims to share with readers the spirit and excellence of this seminal meeting addressing such a pertinent topic, while providing a glimpse into the exciting world of COPD research. Enjoy.
COPD is a very complex disease, with many potential causes and exacerbation factors only recently being recognized and studied. Over the course of two full days, 30 speakers — studying all aspects of COPD — shared their respective research findings and treatments, speculated on future directions, and discussed how their findings compare with those of their colleagues.

Some researchers feel there is an autoimmune component to COPD: many individuals with COPD who have stopped smoking have active inflammation in the lungs, and their COPD may continue to get worse for many years — even after they have quit smoking — due to this ongoing inflammation. This sustained inflammation is thought to be mediated by autoantibodies and autoreactive T cells.

Other scientists are testing genetic theories — there is evidence that a person’s genetic makeup may actually make them more susceptible COPD, and studies have found that COPD is more common among relatives of COPD patients who smoke than unrelated smokers.

Research is also being conducted into “airway remodeling” — these scientists study the actual structural changes that occur in the airways of COPD patients as their disease progresses, and how this affects their quality of life, whether these changes can be reversed, and their effect on patients’ rehabilitation.

Where a person lives and works may also play a big role in whether they develop COPD — some people living in areas with higher pollution rates, or women who regularly cook over open fires, have higher COPD rates than the general population, leading scientists to question whether there is an environmental component to COPD. Industry-related inhaled toxins are also being closely examined for their potential role in COPD.

The differences between men and women may also play a key role in COPD — the lack of research specifically done on large groups of women is one element currently being addressed. There are also scientists conducting studies on animals to better understand COPD and its causes, as well as using animal models to predict COPD progression in humans.

Imaging and diagnostic techniques play a key role in COPD — major advances in radiology, CT-scanning and other imaging techniques are allowing COPD researchers to look even more closely at lungs, bronchioles and blood vessels of patients as they study COPD and its progression.

How to treat COPD is also a key area of research — current studies include the effects of inhaled cortico-steroids, bronchodilators, anticholinergics, surgical interventions, and more. The conference also featured presentations from doctors working directly with patients to self-manage their COPD, and the challenges involved in creating and monitoring these types of self-regulating programs.

The conference presentations covered all these areas and more — from airway remodelling and genetic studies to surgical interventions and the role of COPD research was discussed, as well as new inroads being made into more effective diagnosis and treatments. Presenters also shared findings from “informal” studies and anecdotal evidence, which often provides insight and commonalities between scientists.

After every presentation, attendees were invited to join the discussion and debate — new research findings were compared — and the result was a collaborative, productive and thought-provoking atmosphere for some of the world’s leading researchers to share their increasing knowledge on COPD. Read on for summaries of each speaker’s presentation.
Dr. Paré and his colleagues are working to isolate alleles in candidate genes that contribute to lung function decline in COPD patients. Only 20–25% of smokers develop COPD, and studies have found no significant differences in FEV₁s or FEV₁/FVC between lifelong nonsmoking first-degree relatives and nonsmoking control subject, leading to the hypothesis that multiple genes with small effects likely dictate who will get COPD. Dr. Paré also discussed a “nested case-control” study in the Lung Health Study (LHS), conducted by the National Heart, Lung, and Blood Institute and designed to describe the natural history of cigarette-induced COPD. For the study, a 600-member follow-up group of subjects (300 with fastest rate of FEV₁ decline, 300 with the slowest) were studied to identify biologically plausible candidate genes. Researchers aimed to identify functional and/or tagging single-nucleotide polymorphisms (SNPs) in relevant genes by comparing the allele, genotype and haplotype frequencies in the two groups. Dr. Paré has concluded that gene variants can influence susceptibility for COPD by influencing rate of decline of lung function, and that the interaction between smoking and senescent metabolizing enzymes is present and biologically plausible.

**Molecular Pathogenesis of COPD**

Dr. Barnes is studying the molecular mechanisms of COPD and asthma. The inflammatory profiles of COPD are largely determined by the involvement of different immune cells, which orchestrate the recruitment and activation of inflammatory cells that drive the distinct patterns of structural changes. Dr. Barnes has found increased expression of the transcription factor NF-κB in the airways of patients with COPD during an exacerbation compared to a stable state. NF-κB regulates the expression of cytokines, chemokines, adhesion molecules, proteases important to the inflammatory response in COPD. This suggests that by inhibiting NF-κB several inflammatory genes important in the inflammatory response in COPD may also be inhibited. Dr. Barnes has also determined that while treatment with inhaled corticosteroids does not modify the long-term decline in FEV₁ in patients with COPD, they decrease the number of exacerbations and/or the number of genes addition with long-acting inhaled beta2 agonists reduce symptoms. Defective HDAC in subjects with COPD could be caused by genetic factors, viral infections, or oxidative stress.

**Putting the Patient in Charge: Self-Management in COPD**

In COPD exacerbation, patients have little or no understanding of their symptoms or of warning signs that should result in specific actions. By creating a written self-management plan, COPD patients and health care providers can work together to manage COPD. This type of support program involves collaboratively helping patients acquire the skills needed to carry out disease specific medical regimens, guiding change in health behavior to help adjust their roles for optimal function, disease control, and well being. It includes assessment of progress and education. Dr. Bourbeau feels COPD professionals have failed to recognize variations in the way self-management programs are designed, delivered and evaluated, leading to inappropriate conclusions about the programs’ effectiveness and likelihood of inappropriate application of research results in clinical practice. Success will result in goals of self-management e.g. acquiring key self-management skills and self-health behaviors. Better research is needed to increase understanding of the relative effectiveness of specific components and how to best support COPD patients in self-management. Dr. Bourbeau believes better patient education and early intervention can significantly reduce the burden of COPD.

**Genetics of Rapid Decline in Lung Function**

Dr. Churg is conducting “drug therapy” trials in laboratory mice to determine the pathogenesis of emphysema. He spoke about the protease-antiprotease hypothesis. Briefly, it is postulated that the inflammatory cells release proteases that overwhelm the local antiproteolytic defenses, resulting in proteolytic destruction of connective tissue matrix and eventual emphysema. The question of which cells or proteases are the crucial mediators remains unanswered. Dr. Churg treated these smoke-induced COPD mice with antiproteolytic/anti-inflammatory interventions with good results, but these results so far have not been translated to human subjects. Dr. Churg concluded that in human emphysema, as in mouse emphysema, there are different phases to the disease, and these phases require/respond to different therapies. There is an early reparative phase in humans during which the parenchyma can repair the smoke-induced damage, and a later phase in which it can’t repair it at all. Thus, the timing of the intervention may be crucial to good outcomes. Dr. Churg also concluded that small airway remodeling is a completely separate process, requiring separate treatment.

**UPLIFT and its Meaning for the Treatment of COPD**

Dr. Celli spoke about two key COPD trials. The first is TORCH, which studied the effect of salmeterol and fluticasone propionate with regard to survival in COPD patients. The TORCH study determined that pharmacotherapy with salmeterol plus fluticasone propionate, or the components, reduces the rate of decline of FEV₁ in patients with moderate-to-severe COPD, thus slowing disease progression. The second study — UPLIFT — is a 4-year COPD trial to determine whether tiotropium reduces the rate of lung function decline as measured by FEV₁. UPLIFT found in patients with COPD, therapy with tiotropium was associated with improvements in lung function, quality of life, and exacerbations during the four-year period but did not significantly reduce the rate of decline in FEV₁. Dr. Celli hypothesized that hyperinflation of the lungs may have more of an impact on heart function and oxygen delivery than previously assumed, and the heart plays a greater role in COPD. Dr. Celli suggests there is no more need for placebo-controlled long-term trials, but rather an investigation and evaluation of potential agents.

**COPD: The Autoimmune Paradigm**

Why is it that only 20% of smokers develop COPD? Dr. Cosio hypothesizes that autoimmunity may be the answer to this question. For a long time, it was believed that because neutrophils and macrophages were increased in COPD, they were the only inflammatory cells involved in the pathogenesis of COPD. However, it is now recognized that T-cells are also increased in smokers’ lungs, leading Dr. Cosio to question their role in COPD. Naïve, non-stimulated T-cells do not enter the lung normally; they “home” to the lung upon antigen recognition. Therefore, the traditional inflammation in smokers (neutrophils and macrophages) should be interpreted as an innate immune response to cigarettes, which is then followed by an adaptive response with T-cells. IF-T-cells are responsible for the lung injury and progression of COPD, it would be as a response to an antigenic stimulus originating in the lung induced by cigarette smoking. The role of autoimmunity in COPD could explain the differences in susceptibility, familial predilections, and disease progression in ex-smokers and the systemic effects seen in COPD, and could lead to a more effective therapeutic approaches to the disease.
Harvey O Coxson, PhD
CT Scanning for COPD Phenotypes

Dr. Coxson’s presentation was about quantifying different aspects of computed tomography (CT) scans, which is a non-invasive way to measure the airway wall dimensions of people with and at risk for COPD. Recent advances in CT technology and new computer algorithms have changed the way investigators have measured airways using CT, and it is now hoped that many of the early issues surrounding airway measurements can be resolved.

COPD breaks out into two morphologic areas: parenchymal inflammation (emphysema) and airway inflammation and re-modeling and thickening of airways (small airway disease). These two things interact to produce lower expiratory flow, hyperinflation and gas exchange abnormalities that result in COPD symptoms. The phenotypic expression of these different subtypes of COPD is vital because a therapy designed to modulate the inflammation in airways may be contraindicated in subjects with the emphysema phenotype and visa versa. Therefore, these new imaging techniques are very likely to play a front-line role in the study of COPD and will, hopefully, allow clinicians to phenotype individuals, thereby personalizing their treatment.

Malcolm Johnson, PhD
Novel Molecular Targets in COPDCOPD

Dr. Johnson spoke about advances being made in new treatment drugs for COPD. Super bronchodilators such as Indacaterol/NVA 237 and once-daily 2-agonists or ultra long-acting 2-agonists (LABAs) are currently being investigated for the treatment of asthma and COPD. There are also new long-acting antimuscarinic agents (LAMAs) under development. It is believed that inhalers containing a combination of several classes of long-acting bronchodilator drugs would help simplify COPD and asthma treatment. There are several options for once-daily dual-action ultra LABA+LAMA combination products are currently being evaluated. Another type of bronchodilator being investigated is M3 antagonist-2 agonist (MABA), in which both pharmacologies are present. One such drug is GSK061081, which recently completed Phase 2 trials. Dr. Johnson spoke about restoring steroid sensitivity in COPD using anti-oxidants, p38-kinase inhibitors, PI3-kinase inhibitors (delta, gamma) and HDAC activators. COPD is now recognized by the pharmaceutical industry as the only chronic disease that is increasing in prevalence; researchers must be smart and break out of predictive research patterns.

Seb Johnston, MD, PhD
Viral Infections in COPD

Despite evidence that links respiratory virus infections to COPD exacerbations, the cellular and molecular mechanisms by which viruses cause exacerbations are still not known. Dr. Johnston and his colleagues evaluated the possibility of developing an experimental model of rhinovirus-induced COPD exacerbations to study the effects of rhinovirus infection in COPD patients — often a research gap. They carried out a pilot virus dose escalating study to assess the minimum dose of rhinovirus 16 required to induce experimental rhinovirus infection in subjects with COPD (GOLD stage II). They found that all four subjects developed symptomatic colds with the lowest dose of virus tested, associated with evidence of viral replication and increased pro-inflammatory cytokines in nasal lavage, accompanied by significant increases in lower respiratory tract symptoms and reductions in PEF and FEV1. Dr. Johnston concludes that infections are important in the pathogenesis of COPD exacerbations, and that viruses likely precipitate the majority of COPD exacerbations. Dr. Johnston sees the need for a new experimental model to identify the increased susceptibility and pathogenic mechanisms in COPD. New approaches to treatment will hopefully emerge from better understanding of the role of virus infections in COPD.

David Mannino, MD
The Worldwide Prevalence of COPD and New Risk Factors

Dr. Mannino spoke about the growing burden of COPD. The current method of assessing COPD severity is the GOLD Guidelines for lung function, which rate the severity of COPD on a scale of 0-4, with 0 being defined as “at risk” and 4 being very severe. One of the challenges in using this tool is defining the “lower limit of normal,” as it varies between populations. COPD is both a developed and developing world problem. According to the World Health Organization, COPD will be the fifth leading cause of death worldwide by 2030. Pollution from wood and coal burning is a major cause in developing nations. Dr. Mannino talked about the Plantino 2030. Pollution from wood and coal burning is a major cause in developing nations. Dr. Mannino talked about the Plantino study, which assesses rising COPD rates in Latin America — whether this increase is due to environmental factors, rising smoking rates or other factors is still unclear. Another study, BOLD, found higher levels and more advanced staging of spirometrically confirmed COPD than have typically been reported; but although age and smoking are strong contributors to COPD, they do not explain variations in disease prevalence. New risk factors such as vapor, dust, gas or fume exposure, co-morbidities, gender, socioeconomic factors, location and more are now being studied.
The 2009 COPD Conference, Vancouver BC

Dr. O'Donnell focused on the sex differences in airway structure/function, the ventilatory and perceptual responses to exercise in healthy young women and men, and then on the sex differences in exercise responses with regard to aging, those with mild COPD, and those with moderate to severe COPD. Exercitational breathlessness is greater in healthy women than in age-matched men: 30% of healthy adults >65 years of age experience breathlessness on activity, but this symptom is more common in women. Among patients with COPD matched for FEV1, women report greater dyspnea symptom is more common in women. Among patients with COPD matched for FEV1, women report greater dyspnea.

Most studies investigating COPD have not been designed to assess gender differences. Study groups tend to include far more men than women, or study groups are too small to adequately assess gender differences. Research findings also suggest doctors are more likely to diagnose men with COPD than women. Smoking affects women differently than men; factors such as cigarette brand, inhalation strength and particle deposition must be considered; women who smoke to women — women may have smaller airways and lung volumes, lesser lung diffusing capacity and other physiological differences. Females typically report greater breathlessness during standardized physical tasks than age-matched males, reflecting naturally reduced ventilatory reserve and relatively increased contractile muscle effort requirements in females. Although COPD erodes the ventilatory reserve similarly in both sexes, the sensory consequences during activity are greater in males.

Masaharu Nishimura, MD, PhD
Application of 3D Airway Analysis to COPD Research

Dr. Nishimura is studying structure-function studies in COPD as they relate to lung airway dimension and airflow limitation, reproducibility and heterogeneity, and the contribution of airway disease to airflow limitation. Dr. Nishimura and his colleagues have developed new, original software that allows the measurement of airway dimensions up to the 6th generation at any site in the lung. They determined that airways dimensions significantly correlated with FEV1. They also found the correlation coefficients improved as the airways became smaller in size from the 3rd to 6th generations in the two bronchi. Airway luminal area (A1) is not a pure index of airway disease itself, particularly when measured in vivo, but rather is influenced by several direct and/or indirect factors such as airway thickening, secretions within the airway, and the pressure balance between inside and outside of the airway. The group also applied their new 3D airway analysis to two clinical studies in COPD to assess bronchodilator response COPD. Both studies demonstrate that distal airways rather than proximal airways among the 3rd to 6th generation, are more relevant to functional parameters in COPD.

Denis O’Donnell, MD, FRCPI, FRCP
Physiology of COPD in Men and Women

Dr. O’Donnell focused on the sex differences in airway structure/function, the ventilatory and perceptual responses to exercise in healthy young women and men, and then on the sex differences in exercise responses with regard to aging, those with mild COPD, and those with moderate to severe COPD. Exercitational breathlessness is greater in healthy women than in age-matched men: 30% of healthy adults >65 years of age experience breathlessness on activity, but this symptom is more common in women. Among patients with COPD matched for FEV1, women report greater dyspnea symptom is more common in women. Among patients with COPD matched for FEV1, women report greater dyspnea.

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Dirkje Postma, MD, PhD
COPD In Men and Women: Are They Really the Same Disease?

The development of chronic airflow obstruction in smokers is highly variable. A small percentage of COPD patients inherit severe alpha 1-antitrypsin deficiency, but identifying the genetic determinants of COPD risk is essential to understanding COPD. Dr. Silverman and his colleagues conducted the first-ever genome-wide association study in COPD to try to identify these genes. This involved four different groups: beginning

Sanjay Sethi, MD
Bacterial Infections in Acute Exacerbations

Dr. Sethi’s presentation was on new approaches to treating bacterial infections in acute exacerbations in COPD. Dr. Sethi and his colleagues conducted a prospective study to test their theory that the acquisition of a new strain of a pathogenic bacterial species leads to changes in airflow and systemic inflammation, which in turn results in an increase in respiratory systemic symptoms resulting in strain-specific immune response antibodies with elimination of the infecting strain. The study collected clinical information and sputum samples for culture both monthly and during exacerbations from 81 outpatients. Using molecular typing, an exacerbation was diagnosed at 33% of the clinic visits that involved isolation of a new strain and during exacerbations from 81 outpatients. Using molecular typing, an exacerbation was diagnosed at 33% of the clinic visits that involved isolation of a new strain at which no new strain was isolated, supporting the causative role of new strains of bacteria in COPD exacerbations. Dr. Sethi concludes that the majority of COPD exacerbations are infectious. More research into bacterial-viral, environmental interaction is needed, as well as into molecular detection and quantification of infectious pathogens. The virulence of these pathogens must be considered, and weighed against the patient’s susceptibility to infection.

Frank Sciurba, MD, FCCP
New Frontiers in Interventional Bronchoscopy in COPD

Dr. Sciurba discussed developments in COPD treatment. Lung volume reduction surgery (LVRS) which involves removing a mass from the lung to alleviate pressure, has been successful. However, fewer than 200 procedures were performed in the US last year. Dr. Sciurba also spoke about bronchial valves, whereby a valve is surgically implanted in the lung to expand the bronchi; trials so far have shown some success but the procedure has not been approved by the FDA. Another technique is Biologic Lung Volume Reduction (BLVR), which injects chemicals that form a hydrogel to reduce lung volume by permanently collapsing and sealing the diseased areas of the lung. Dr. Sciurba also discussed bronchial fenestration, in which a direct connection between the bronchus and the collarattely ventilated lung parenchymal region is made using noncollapsible bronchial stents to create new conducting expiratory airways, and a new technique that uses a catheter to put vapour in the lungs, which causes the diseased portion of the lung to reduce in volume. Dr. Sciurba sees novel approaches emerging and evolving through Phase 3 trials that could provide a tool chest of options for treating COPD.

Edwin Silverman, MD, PhD
Genetics of COPD

The development of chronic airflow obstruction in smokers is highly variable. A small percentage of COPD patients inherit severe alpha 1-antitrypsin deficiency, but identifying the genetic determinants of COPD risk is essential to understanding COPD. Dr. Silverman and his colleagues conducted the first-ever genome-wide association study in COPD to try to identify these genes. This involved four different groups: beginning with a homogeneous case-control cohort from Norway, of which they evaluated the top 100 single nucleotide polymorphisms in the family-based International COPD Genetics Network. They then evaluated the polymorphisms that showed replication in subjects from the US National Emphysema Treatment Trial, and controls from the Normative Aging Study, and then in a fourth cohort of extended pedigrees from the Boston Early-Onset COPD population. This study identified two major susceptibility loci. Dr. Silverman feels future genetic studies of COPD heterogeneity must include more comprehensive candidate gene panels and genome-wide association data. There also need to be larger samples sizes and more sophisticated statistical modeling.
The 2009 COPD Conference, Vancouver BC

COPD is not just a disease of the lungs. In early and moderate stage COPD patients, CVD and cancer are the leading extra-pulmonary complications. In advanced patients, osteoporosis, cachexia, and peripheral muscle weakness are leading complications. Dr. Sin and his colleagues are studying what links these co-morbidities by examining relative risks and population-attributable risks in COPD patients. Much of the existing genetic research into COPD cannot be reproduced in subsequent experiments, leading Dr. Sin and his colleagues to seek new answers. One theory is that the persistent lung inflammation of COPD promotes the translocation or "spillage" of inflammatory molecules from the lungs into the rest of the body, which then stimulate other organs to release excessive acute-phase proteins, inflammatory cells, and secondary cytokines into general circulation, resulting in persistent low-grade systemic inflammation. If this were the case, it would permit the use of systemic measurements as potential biomarkers of disease. Blood-based biomarkers would help researchers better understand the pathophysiology of COPD and how it is linked with co-morbidities such as CVD and osteoporosis. It would also allow for blood-based tests to evaluate new compounds in COPD. Finding such biomarkers will require a new approach combining proteomics, immunomassays, discovery and replication.

COPD and Extra-Lung Manifestations

Robert Stockley, MD, DSc, FRCR
COPD: Lessons Learned from Alpha One Antitrypsin Deficiency

Alpha 1-antitrypsin protects the lungs from the neutrophil elastase (NE) enzyme, which can disrupt connective tissue, and from damage caused by protease enzymes, such as trypsin, that can be released as a result of an inflammatory response to tobacco smoke. Alpha 1-antitrypsin deficiency (AATD) leads to a chronic uninhibited tissue breakdown, which causes the subsequent degradation of lung tissue. The effects of NE include emphysema, mucus gland hyperplasia, mucus secretion, epithelial destruction and leakage, reduced CBF, proinflammatory and immune parries. Dr. Stockley has found that where neutrophils are migrating through the lung, some local NE activity (from a released azurophil granule or released from cell membrane association) could be beneficial, but that free NE in lung secretions are harmful. The location of the lung damage — lower or upper lung — appears to play a role in COPD progression. Neutrophils in COPD patients migrate more quickly and erratically than those in healthy lungs, and that the more complex the migration patterns, the higher the level of damage in COPD. Neutrophils have also been implicated in other manifestations of COPD, since experimental application of NE can produce many of the features of patients with this syndrome.

Rubin Tuder, MD
COPD and Senescence

The lung, like any other organ, deteriorates as the human body ages, which is a process that alters basic controls involved in cell growth, cell maintenance, and cell death. The failure of somatic cell maintenance and repair as the body ages is a key factor in COPD. Dr. Tuder is studying the role of senescence — the exhaustion of cell replication in vitro (G1), characterized by enlarged cells with flattened cytoplasm, metabolically active, with "resistance" to modified by intervention. One of the main goals of the ECLIPSE study is to identify markers for meaningful subtypes of COPD, such as emphysema, asthma and chronic bronchitis. COPD is a multicomponent disease involving hyperinflation of the lungs, structural changes, mucociliary dysfunction and more. The ECLIPSE study will monitor participants’ pulmonary function measurements, computed chest tomography, biomarkers (in blood, sputum, urine and exhaled breath condensate), health outcomes, 6-minute walking distance and other outcomes. Dr. Tuder and his colleagues hope the study provides researchers a greater understanding of COPD and, ultimately, defines the predictors that monitor disease progression in individuals with different COPD traits.

Emerging Biomarker Studies in COPD: the ECLIPSE Study

Joanne Wright, MD
COPD and Pulmonary Hypertension

Nearly 8% of people over 40 will develop COPD in their lifetime, a total of 280 million people. 24.3% of smokers will develop moderate to severe COPD. Pulmonary hypertension, which has been attributed to emphysematous destruction, hypoxia and the alteration of time constants affecting perfusion, develops in approx 6% of patients with COPD. Dr. Wright hypothesizes that cigarette smoke acts directly upon the pulmonary vasculature to induce upregulation of vasoactive mediators, pulmonary arterial remodeling with increased muscularization, and alteration of the vasconstrictor/vaso dilation balance. She and her colleagues studied guinea pigs to assess whether these mediators could be implicated in the structural remodeling of the arterial vasculature and increased pulmonary arterial pressure caused by chronic cigarette smoke exposure. Guinea pigs were exposed to daily cigarette smoke for 6 months and their pulmonary arterial pressures were measured. They concluded that chronic smoke exposure produces increased vasoactive mediator expression in the small intrapulmonary arteries and that such mediators are associated with vascular remodelling, increased muscularization, and endothelial dysfunction, with the ultimate production of pulmonary hypertension.
On February 7th, 2009, researchers, clinicians, friends and family gathered at the Vancouver Club to honour Dr. James Hogg. This elegant dinner — timed to coincide with the 2009 COPD Conference — was a true tribute the combination of brilliance, perseverance and humility that Dr. Hogg exhibits in all aspects of his life.

A recurring theme soon became evident in the presentations by each of the 30-plus speakers at both the COPD conference and the tribute dinner: Dr. Hogg’s commitment to excellence, his ability to challenge and inspire his students and colleagues, and his quiet, courteous manner combine to make him a world-renowned and respected scientist, researcher and friend.

Dr. Hogg has trained many talented individuals who have gone on to hold faculty positions, research chairs, and conduct bold research... and he continues to inspire students, post docs, colleagues in the international community, and his fellow faculty members. Dr. Hogg works with all levels of staff and faculty to bring about progress by recognizing that it is people, not facilities, that make a vibrant research organization.

Dr. Hogg’s origins lie in Manitoba, where he attended university, earning his MD from the University of Manitoba in 1962. Upon graduation, Dr. Hogg joined the Canadian Armed Forces and was posted to Greenwood, NS, where he served as an army doctor. In 1969, he earned his Ph.D. in Experimental Medicine from McGill University, and then completed residency training in Anatomic Pathology at the Massachusetts General Hospital and McGill University.

In 1977, Dr. Hogg was recruited to Vancouver by St. Paul’s Hospital and the University of British Columbia. Both he and Dr. Peter Paré, his post-doctoral fellow at the time, arrived to build a research laboratory in the same interdisciplinary tradition that they had experienced at McGill University. The fledgling Pulmonary Research Laboratory grew steadily over the years and gradually expanded into the McDonald Research Laboratories (MRL).

Under Dr. Hogg’s direction, excellent researchers were recruited and integration of the Pulmonary and Cardiovascular Research Groups lead to the formation of the iCAPTURE Centre in 2000. The Centre focuses on dissecting the complex genetic and environmental influences that determines susceptibility to diseases of the heart, lung and vascular systems, particularly those with a prominent inflammatory or infectious manner. In 2003 the Centre was re-named the James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research recognizing the immense contribution of Dr. Hogg to its success.
The James Hogg iCAPTURE Centre

The James Hogg iCAPTURE Centre (Imaging, Cell Analysis, and Phenotyping Toward Understanding Responsive, Reparative, Remodelling, and Recombinant Events) at St. Paul’s Hospital, is a UBC Senate-approved research centre supported by the Faculty of Medicine of UBC and Providence Health Care.

iCAPTURE is built on a 30-year history of excellence: back in 1977, a young scientist by the name of James Hogg was recruited to St. Paul’s from Montreal to found the Pulmonary Research Lab. Along with Dr. Peter Paré, Dr. Hogg established a world-class research facility that immediately attracted top international researchers. The lab was re-christened the McDonald Research Lab in 1986. In 2000, $21 million in funding from the Canada Foundation for Innovation and its partners led to the creation of the James Hogg iCAPTURE Centre.

The Centre now includes over 270 scientific personnel devoted to finding solutions for inflammatory and infectious heart, lung and blood vessel diseases. As the innovation and discovery engine of the Heart + Lung Institute at St. Paul’s Hospital, the iCAPTURE Centre works seamlessly with other units within Providence Health Care, including the Pacific Lung Health Centre, the Centre for Health Evaluation and Outcomes Sciences (CHEOS), and the St. Paul’s Heart Centre.

Led by Director Dr. Bruce McManus and an Executive Team, investigators, trainees, and staff in the iCAPTURE Centre are using the best available technology to image and measure changes in molecules, cells, tissues, organs, and whole organisms, including patients, to understand the link between our genes and environments in causing heart, lung, and blood vessel diseases.

GlaxoSmithKline Inc. (GSK), one of the world’s leading research-based pharmaceutical, vaccine and healthcare companies, is devoted to discovering and developing new and innovative medicines and vaccines for people around the world. GSK is a top investor in Canadian research and development, contributing more than $156 million in 2008 alone.

COPD is projected to be the third-leading cause of death and responsible for approx. 4.5 million deaths by 2020. GSK is committed to furthering the understanding and treatment of COPD and to supporting research initiatives that will lead to improved health outcomes for people who suffer from this disease.

GlaxoSmithKline extends its congratulations to the organizing committee of the “COPD 2009: Reactive Past, Preventive Future” conference for their vision and commitment to this innovative and important meeting. Together, we will strive toward a future of enhanced diagnosis, management and treatment of COPD.

For more information on GSK Canada, visit www.gsk.ca
Living Well with COPD — Public Forum

The public forum — Living Well with COPD — was held February 5, 2009 at the Sheraton Wall Centre in Vancouver in conjunction with the BC Lung Association. The event was hosted by Dr. Art Hister, and over 300 COPD patients attended. Two world-renowned respiratory health experts — Dr. Denis O’Donnell and Dr. Bart Celli — spoke and then answered questions from attendees, and several participants also shared their experiences with COPD. It was an afternoon of learning and sharing that demonstrated that putting the best available advice into practice allows people with COPD to live full lives.

Dr. O’Donnell spoke about the enormous benefits of exercise in COPD rehabilitation — it’s been shown that exercise can have 2-3 times the impact of drug therapy on COPD symptoms. Once COPD patients have maximized their medication, the most important next step is to be enrolled in supervised exercise program — this is the principle behind rehabilitation.

COPD is characterized mainly by airway narrowing — smoke inhalation causes damage and the airways begin to narrow. One consequence of this is air trapping. The resulting shortness of breath leads to inactivity — people begin to abandon activities they used to enjoy and begin adapting their lifestyle to avoid activity. This is disastrous, as it begins a downward spiral. The leg muscles begin to waste in a process known as deconditioning. The structure of the muscle actually changes, and its ability to perform work diminishes — putting COPD patients at risk for other illnesses like diabetes and osteoporosis.

The key to breaking the cycle is exercise re-conditioning. Any muscle — even in an 80-year-old — can benefit from targeted exercise regime. Studies have show repeatedly that an exercise program will improve COPD symptoms, reduce exacerbations and hospitalizations. Exercise is the best intervention there is.

Once patients have completed a supervised exercise rehabilitation program, the most important thing is maintenance. Fewer than 2% of Canadians have access to a supervised rehabilitation program, so there is an increasing emphasis on home-based rehabilitation programs. COPD patients should work with their health care providers to develop an exercise maintenance program that they can follow at home.

Dr. O’Donnell also stressed the importance of early and aggressive treatment of exacerbations, or flare-ups. The best way for COPD sufferers to avoid exacerbations is to take all medication as prescribed, use inhalers, and exercise regularly.

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COPD patients should work with their doctor to develop an action plan to recognize and deal with exacerbations. The Canadian Lung Association is currently developing a nationwide program to help devise action plans. (Visit www.lung.ca for more information.)

Dr. Celli spoke about new advances in COPD research and treatment. COPD is the only chronic illness that is increasing in prevalence, yet it does not receive nearly as much attention as other illnesses such as cardiovascular disease and cancer. This is slowly changing as patients and researchers begin to speak out about COPD, and as the results of several large-scale trials become available.

The UPLIFT trial — done in 49 countries and comprising over 6,000 people — found that most people with COPD respond to bronchodilators — over 50% have a 200 mL improvement in their airflow rates. The TORCH trial, large-scale three-year COPD trial, has found that the number of flare-ups is reduced by 25% for patients who take their medication religiously.

Dr. Celli emphasized that medications are very effective in controlling COPD exacerbations and the rate of decline, but reminded participants that lungs are just one part of the body. A person’s overall health contributes to COPD maintenance in many ways — high blood pressure and cholesterol should be monitored, and keeping active is essential.

The future of COPD research and treatment is promising. Researchers are currently looking for “markers” that predict COPD with the hope of being able to diagnose COPD earlier. It’s important that COPD patients participate in trials to help find out if there are in fact specific markers. Dr. Celli called on COPD patients across the world to unite and work together to fight COPD.
I've found that two puffs of marijuana a day helps me as much as my puffer — what is the medical thinking on this? Is there any place for marijuana in COPD treatment?

Dr. O'Donnell: Marijuana inhalation can have an immediate effect on the smooth muscles, and relax them short-term, but over the long-term it is harmful. Studies show long-term marijuana smoking causes destructive emphysema, so I would not recommend it.

Are there any magic tricks I can use to inspire the person I love to start exercising?

Dr. O'Donnell: It's all a question of a new, operational habit. It can be difficult to start, but once it becomes entrenched, it gets easier. The biggest mistake people make is to aim too high. The easiest way to start is with a small goal, even small goals like, "I'm going to do six minutes of activity the first day — take a break the second day, then the third day do a bit more. Any exercise is better than no exercise. It's also important to do something you enjoy. Walking is superb exercise. Start modestly and be happy with small victories. Be patient.

I had four lung infections last year. Should I be worried about taking antibiotics too frequently?

Dr. O'Donnell: Did you use same antibiotic every time? If so, there is a danger of developing resistance to the antibiotic. We try to rotate the type of antibiotics we prescribe, and not prescribe them more than once every three months.

If you have moderate lung damage, and have been smoking two packs of cigarettes a day, is there any point in stopping?

Dr. Celli: Stopping smoking at any point is beneficial — and not just for COPD symptoms. Your lung function will improve and the rate of decline will slow. Smoking also causes other diseases like lung cancer, bladder cancer, heart disease — quitting will help fight those other diseases as well. Earlier is better.

In terms of whether it’s better to cut down on how much you smoke — smoking less is better than smoking more, of course, but quitting is much better.

How important are immunizations like flu shots and the pneumovaccines? How often should I get one?

Dr. O'Donnell: Studies have shown the annual flu vaccine is effective in preventing incidences of influenza. People with COPD are at risk for bacterial infections when they get the flu, so if you reduce incidences of the flu, your chances of getting a bad bacterial flare-up are significantly reduced.

The pneumovaccine is a bit trickier — if you have severe COPD, it's recommended you get one every five to 10 years. Talk to your doctor about what is best for you.

Dr. Celli: A small dose of alcohol is OK — however, overdoing it can lead to aspiration and an increased propensity for infection, liver damage, etc. Moderation is the key.

Does alcohol use affect COPD?

Dr. Celli: There is a condition known as alpha 1-antitrypsin deficiency — this is a genetic disease that is quite frequently observed in the general population that seems to predispose people for COPD. Even non-smokers with this alpha 1-antitrypsin deficiency can develop COPD.

So we know genetics can play a role. There are researchers studying right now and it's exciting — imagine if we found what made some people genetically resistant to COPD? We could mimic that to treat COPD sufferers.

Are some people naturally pre-disposed to get COPD?

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Is there a genetic component to COPD?

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Dr. O'Donnell: Exacerbations are the enemy of rehabilitation! It can be very discouraging for people who are on exercise program to have an exacerbation, as it sets them back to the baseline.

In people with more advanced COPD, an exacerbation can floor you for several weeks. Aggressive treatment post-exacerbation can help, and a decrease in the amount of exercise, but don’t stop your activity completely. Just reduce it. Avoiding inactivity is the best solution. Unfortunately, exacerbations do cause further damage — pulmonary function over time is affected more by more flare-ups — which is why early and aggressive treatment is so important.

Will I ever be able to stop taking my COPD medication sometime in the future?

Dr. Celli: It’s very hard to stop. In the experience of health care professionals, staying on your medication is the most effective way to avoid exacerbations. The data shows that if you stop taking your inhaled steroids, you get exacerbations. Unless you have severe side-effects aside, stick with your meds.
Meet the Forum Speakers

Dr. Denis O’Donnell’s presentation was all about ways to take control of your COPD. Dr. O’Donnell is a Professor of Medicine, Physiology, and Kinesiology/Health Studies at Queen’s University in Kingston, Ontario; Director of the Respiratory Investigation Unit at Queen’s University, Director of the Pulmonary Rehabilitation Program, and current Chair of the Canadian Thoracic Society COPD Guidelines Committee.

Dr. Art Hister is a family physician, broadcaster and media doctor. He is the host of “House Calls” on the Canadian Corus Radio Network, is a daily health analyst on Global TV (BC) and CKNW’s Morning Show as well as a weekly analyst on Up All Night on BBC 5 and Shaw Cable TV in BC.

Dr. Bart Celli gave a great presentation on what new research is revealing about COPD, and answered participant questions on a range of topics. Dr. Celli is a Professor of Medicine at Tufts University and Chief of the Division of Pulmonary and Critical Care at St. Elizabeth’s Medical Center in Boston. Dr. Celli trained in Pulmonary and Critical Care Medicine at the Boston University School of Medicine.
10 Things You May Not Know About COPD

1. COPD stands for Chronic Obstructive Pulmonary Disease, and is a serious lung disease.

2. COPD progresses slowly, and over time, makes it very difficult to breathe.

3. The World Health Organization (WHO) estimates 600 million people worldwide have COPD.

4. COPD will be the third-leading cause of death worldwide by 2030.

5. Smoking is the #1 COPD risk factor: 5.4 million people died from tobacco use in 2005.

6. Tobacco-related deaths are projected to increase to 8.3 million deaths per year by 2030.

7. More than half of COPD sufferers have not been diagnosed, leading to a greatly increased burden.

8. The most common symptoms of COPD are breathlessness, excessive sputum production, and a chronic cough.

9. It’s critical those at risk or displaying symptoms take a breathing (or lung function) test called spirometry.