



Alpha-1 Canada Community News



September 2010

What's New at
www.alpha1canada.ca

- **Baxter International Inc. acquires exclusive right to distribute Kamada's Glassia™ alpha-1 augmentation therapy in Canada**
- **Ontario withdraws funding for augmentation therapy, Join the fight to reinstate**

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Update on Ontario government funding for augmentation therapy

On August 30th Alpha-1 Canada was finally able to meet with officials from the Ontario Drug Benefit Program (ODBP) about alpha-1 antitrypsin augmentation therapy reimbursement. Present at the meeting were Diane McArthur, the new Executive Officer of the ODBP (Helen Stevenson's replacement) and Brent Fraser, Director, Drug Program Services. Alpha-1 Canada was represented by Dr. Ken Chapman, Chair of our Medical Advisory Board; Ben Faienza an Alpha-1 Canada board member who is also Vice President of Canadian Operations at i3 Innovus, one of the world's largest health economics and outcomes research compa-

nies; and our Executive Director, Jim Mundy.

To make a long story short, Jim made it clear that we found it unacceptable that patients are losing lung function they will never recover as this process continues into its third year. Ben pointed out the lack of transparency and communication missteps in their process. Dr. Chapman spoke at length about the positive outcomes of augmentation therapy that he and other researchers have demonstrated.

The government representatives seemed to be truly unaware of the research Dr. Chapman referred to. Ms. McArthur agreed to review any evidence we

could provide before making a final decision. Dr. Chapman, bless his heart, said that through Alpha-1 Canada, he would provide the evidence they needed to make a positive decision.

Although there is still much to do, we are happy to say that this is the first positive news we have been able to share on this issue. We will continue to keep you posted.

It is also our hope that the information Dr. Chapman provides will form the basis for submissions by Alpha-1 Canada to other provincial governments that do not currently provide reimbursement for augmentation therapy.

Pfizer Agrees To Buy FoldRx in Rare-Disease Treatment Expansion Effort

by Jim Mundy

Earlier this month, Pfizer Inc. agreed to buy closely held FoldRx Pharmaceuticals Inc. as it looks to expand into medicines for rare disorders.



FoldRx, based in Cambridge, Massachusetts, is focused on developing treatments for conditions which, like alpha-1 antitrypsin deficiency, are

caused by the improper folding of proteins. Although FoldRx is not currently working on a treatment for alpha-1 antitrypsin deficiency, according to their web site, their process is, "readily adaptable to other disease-causing mutant cargo proteins, including variants of α 1-antitrypsin (emphysema), hERG (long QT syndrome), and glucocerebrosidase (Gaucher's disease)."

Other large pharmaceutical companies are also looking to rare diseases as patents on blockbuster drugs begin to expire. The deal fits with Pfizer's new strategy of

focusing on medicines for rare diseases, Geno Germano, head of Pfizer's specialty care unit, said. Pfizer set up a research division in June focused on developing medicines for orphan diseases, classified in the US as conditions affecting less than 200,000 people. More than 30 million Americans have one of 6,000 orphan diseases, according to the National Organization for Rare Disorders. Canada still does not have an orphan drug strategy or an official government definition of a rare disease. The CORD day of action on *continued on page 2*

Pfizer Agrees To Buy FoldRx in Rare-Disease Treatment Expansion Effort

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Parliament Hill at the end of September (see page 3) is designed to change that.

"Within our research organization we established a specific research unit focused on rare disorders and this fits nicely into that area of focus," Germano said. "Rare diseases are an aspect of our portfolio that we think is very attractive, and we are eager to see and continue development."

Pfizer, the world's largest drug maker, contacted FoldRx only weeks ago after one of its researchers saw a scientific poster presented by the company, Richard Labaudiniere,

FoldRx's chief executive officer, said. He said the company was founded in 2004 from a technology project developed at the Scripps Research Institute.

Pfizer is looking to make



acquisitions to help offset some of the revenue it will start losing next year when generic copies enter the market of its Lipitor cholesterol pill, the world's top-selling prescription medicine with US \$11.4 billion in 2009 sales.

FoldRx's most advanced treatment, tafamidis meglumine, is in the final stages of testing required to get regulatory approval in the U.S. to treat transthyretin amyloid polyneuropathy, a fatal disorder of the nervous system that affects about 8,000 people worldwide, Labaudiniere said.

FoldRx is also working on drugs in earlier stages of testing for Parkinson's disease, Huntington's disease, cystic fibrosis, and a rare heart condition called transthyretin amyloid cardiomyopathy. All of its research is focused on developing chemical compounds, rather than injectable biologics.

New class of treatment for COPD may be available in Canada soon

by Jim Mundy

Nycomed GmbH, kicked off the German market launch of Daxas® (Roflumilast) in Oranienburg on September 1, 2010, making Germany the first country to market the medicine. Daxas® (Roflumilast) is a proprietary selective phosphodiesterase 4 (PDE4) enzyme inhibitor that was developed by Nycomed to treat COPD.

Daxas® (Roflumilast) is a once-a-day oral tablet, and is the first in a new class of treatment for COPD. It is indicated for maintenance treatment of severe COPD (FEV1 post-bronchodilator less than 50% predicted) associated with chronic bronchitis in adult patients with a history of frequent exacerbations as an add-on

to bronchodilator treatment.

According to World Health Organization (WHO) estimates, 80 million people have moderate to severe COPD worldwide, including many people with alpha-1 antitrypsin deficiency. More than 3 million people died of COPD in 2005, which corresponds to 5% of all deaths globally. The WHO predicts that total deaths from COPD could increase by more than 30% in the next 10 years unless urgent action is taken to reduce the underlying risk factors, especially smoking.

In Canada, approximately 500,000 people over the age of 35 have been diagnosed with COPD, and it is estimated that an almost equal number of middle-

aged Canadians may also have COPD, but are not aware of it. It is estimated that by 2020, COPD will be the third leading cause of death worldwide.

"Roflumilast improves lung function on top of bronchodilation and over and above concurrent COPD treatments by acting on the underlying inflammation," says Dr. Andrew McIvor, Professor of Medicine, McMaster University, Firestone Institute for Respiratory Health, St. Joseph's Healthcare.

"Considering, the nature of the disease and its affect on people's lives, this presents a very exciting new option for those of us treating patients."

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Tip of the month

Sing, sing a song!

Even off-key, singing helps focus the breath...and that means less stress.

8 Breathing Tips for People with COPD

Health.com recently posted on their web site eight healthy habits, from eating right to exercising, that can help you breathe easier if you have COPD.

Click [here](#) to read more.



Create Awareness

On behalf of Alpha1 Canada we strongly encourage you to join CORD's Annual Action Day on Parliament Hill on September 30, 2010. You can also meet the newest member of our team, Vanessa, who will be attending this year's day of action as well as CORD'S Annual Conference.

Joining with other rare disease patient advocates will provide a strong common voice to advocate for health policy and a healthcare system that works for those with rare diseases.

It will also give a voice to Alphas and create an opportunity to meet other Canadians, from coast to coast, for support and information.

Please do get in contact with us to share your experience should you have the opportunity to attend. We'll look forward to hearing from you.

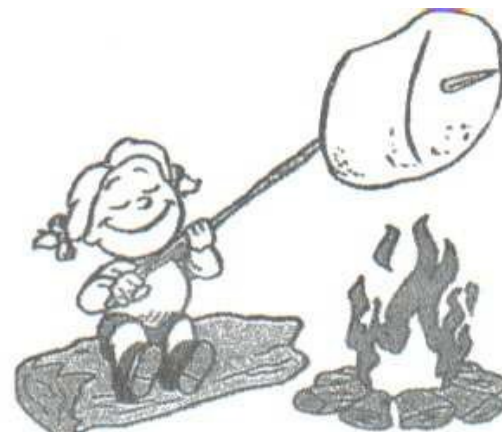
Wood Smoke Health Effects

by Vanessa McLaughlin

While summer doesn't 'officially' end until September 21st, the recent drop in temperature suggests otherwise. If the cold evenings are not sending you inside, perhaps you're keeping warm by a fire. However, if you are burning wood, you are exposing yourself, your family and your neighbours to harmful compounds, including carcinogens.

The belief that wood smoke, being a natural substance, is not dangerous to humans is contrary to recent studies and the knowledge that these fires emit significant quantities of known health-damaging pollutants. Microscopic particles of smoke are so small they get lodged deep in the lungs and can cause coughing, wheezing, shortness of breath and a tight feeling in the chest.

Even low concentrations and short-term exposure can affect those most sensitive to wood smoke – people with heart or lung disease, such as asthma and chronic obstructive pulmonary disease (COPD) whether caused by alpha-1 antitrypsin deficiency or not. People with diabetes may be at increased risk because they may have underlying cardiovascular disease. Older adults are sensitive to air pollution, scientists suspect, because they may have undiagnosed heart or lung disease. Children are sensitive because their lungs are still developing. Long-term exposure can reduce lung function and cause bronchitis and premature death.



A recent study further found that exposure to wood smoke may increase the risk of COPD, particularly among smokers. Breathing in wood smoke, either through home heating, cooking, or ambient outdoor pollution, was associated with a twofold increased risk of airflow obstruction, according to Yohannes Tesfaigzi, PhD, of Lovelace Respiratory Research Institute in Albuquerque, N.M., and colleagues. They reported their findings in the American Journal of Respiratory and Critical Care Medicine. You can read the abstract of their study in our 'Interesting Research' section on page 6.

Interestingly, COPD is common in women in developing countries, probably due to daily cooking over open wood fires.

You can reduce your exposure to wood smoke by avoiding burning wood and keeping your windows closed if your neighbour is wood-burning. Additionally, wood when burned inside also affects air quality and releases pollutants. If you like the cozy feel of a fire, consider switching to a nat-

ural gas fireplace. You can also install a HEPA air filter which reduces the amount of wood smoke in your home. Lastly, install a carbon monoxide (CO) detector in your home as wood smoke contains a mixture of substances, one of which is carbon monoxide. Carbon Monoxide is colourless, practically odorless and tasteless, so you can't detect it on your own.

If you would like more information, please visit the following web sites:

[Residential Wood Heating](#) - A government of Canada website that offers Canadians an excellent range of educational resources on reducing residential wood burning emissions.

[Indoor Air Quality](#) - The Lung Association's web site offers tips to help Canadians reduce exposure to indoor air pollutants in the home.

[Air Pollution from Wood-burning Fireplaces and Stoves](#) - A Toronto Public Health report that describes the emissions from burning wood in the home and their potential health impacts.

Upcoming research studies on Alpha-1 related liver disease

by Vanessa McLaughlin

I recently invited you to join in on a conference call given by Alpha-1 Foundation President & CEO John Walsh (pictured below).



Unfortunately, I did not provide you with the correct participation code and most of you were unable to listen in. This is unfortunate as there were 112 people on this call. Being one of these people, I would like to provide you with the Alpha-1 Foundation's upcoming research studies on Alpha-1 related liver disease as well as their new liver initiative. Most of the information discussed can also be found in the Foundation's Report to the Liver Community. Please click [here](#) to read the report.

The evidence is growing that Alpha-1 liver disease in adults is increasing as Alphas are living longer than they did before current therapies for lung disease were available. While this is good news, it also means that more Alphas will come down with liver disease which, as John explained, can be devastating

for families. It also means that studies are needed on the natural history of liver disease in Alphas. Why do some Alpha-1 adults develop severe liver disease with little warning? How do these Alphas differ from those who live full lives without liver symptoms? How can we track changes that will differentiate a "normal" Alpha-1 liver from a sick liver, and provide earlier detection of liver disease? The Foundation is supporting the grant requests from two institutions now seeking funding from the US National Institutes of Health (NIH) for these desperately needed studies.

Promoting research studies on the natural history of Alpha-1 liver disease is part of a liver initiative the foundation hopes to launch shortly. The initiative came about when the Foundation convened a panel of Alpha-1 experts in May 2010 to recommend priorities for the Foundation's efforts on liver disease. The liver initiative will also ask researchers for Requests for Applications for Grants to fund clinical research on Alpha-1 liver disease, especially in adults; seek partnerships with the NIH and others for co-funding grants; and develop and publish clinical guidelines for healthcare professionals on testing for Alpha-1 liver disease.

Encouraging news can also be found with The Alpha-1 Project, a venture philanthropy program to promote research that identifies new targets for therapeutic interventions with the potential of controlling or curing

the liver and secondarily the lung disease of Alpha-1. The Foundation are hopeful of finding new treatments for Alpha-1 that cannot be developed by academic investigators and require the help of biotechnology companies and the pharmaceutical industry.

Basic research studies have also identified promising new drug targets and potential therapies for Alpha-1. Among the most exciting are:

- ◆ surrogate compounds that are similar to the alpha-1 protein, and that might protect lungs from damage;
- ◆ stem cell and gene therapy, which could allow the body to produce normal alpha-1 protein, or perhaps even to grow normal tissue to repair damaged lungs or livers;
- ◆ and small molecules that might actually correct the misfolded alpha-1 protein, allowing the protein to be secreted normally from the liver cell and circulated through the body.

The Alpha-1 Foundation has been supporting research on Alpha-1 liver disease for more than a decade and is committed to expanding liver research with renewed energy and interest. They urge all Alphas to unite as a community and take every opportunity to create awareness in order to multiply their efforts.

Education Days

The Alpha-1 Association holds mini-conferences called Education Days in the United States throughout the year. On October 23rd, 2010 an Education Day will be held in Seattle, WA making it accessible for Western Canadians living near the border.

Alpha-1 Education Days are a unique opportunity for one to obtain access to educational programs, materials, literature and meet other Alphas.

To register for an Education Day today, please click [here](#).



On Facebook? Join us.

Last month, we invited you to join our Alpha-1 Antitrypsin Deficiency Canada Inc. page. We've become 'liked' by a few more fans and encourage you to join us if you haven't done so already.

Come read and discuss current events, write on our wall, meet new Alphas and much more!

INTERESTING RESEARCH

The following are summaries (abstracts) of recent studies of Alpha-1 and COPD. Please note that Dr. Bourbeau (pictured below), who is a member of Alpha-1 Canada's Medical Advisory Board, is the author of the study in the second abstract and a co-author of the third one.



Because of copyright law we can only provide abstracts, if you want to read more check and see if your local library has these journals on their shelves.

An autophagy-enhancing drug promotes degradation of mutant alpha1-antitrypsin Z and reduces hepatic fibrosis.

Hidvegi T, Ewing M, Hale P, Dippold C, Beckett C, Kemp C, Maurice N, Mukherjee A, Goldbach C, Watkins S, Michalopoulos G, Perlmutter DH. Department of Pediatrics, University of Pittsburgh School of Medicine, Pittsburgh, PA USA.

Science. 2010 Jul 9; 329 (5988):154-5.

Abstract

In the classical form of alpha1-antitrypsin (AT) deficiency, a point mutation in AT alters the folding of a liver-derived secretory glycoprotein and renders it aggregation-prone. In addition to decreased serum concentrations of AT, the disorder is characterized by accumulation of the mutant alpha1-antitrypsin Z (ATZ) variant inside cells, causing hepatic fibrosis and/or carcinogenesis by a gain-of-

toxic function mechanism.

The proteasomal and autophagic pathways are known to mediate degradation of ATZ. Here we show that the autophagy-enhancing drug carbamazepine (CBZ) decreased the hepatic load of ATZ and hepatic fibrosis in a mouse model of AT deficiency-associated liver disease.

These results provide a basis for testing CBZ, which has an extensive clinical safety profile, in patients with AT deficiency and also provide a proof of principle for therapeutic use of autophagy enhancers.

Making pulmonary rehabilitation a success in COPD.

Bourbeau J; Respiratory Epidemiology and Clinical Research Unit, Montreal Chest Institute.

Swiss Medical Wkly. 2010 Sep 1;140:w13067. doi: 10.4414/smw.2010.13067.

Abstract

A truly successful pulmonary rehabilitation entails implementing physical activity maintenance. This article reviews the current knowledge on pulmonary rehabilitation and the expected benefits, the setting, the relationship between self-management and pulmonary rehabilitation, in order to develop and implement clinically-effective physical activity maintenance interventions.

The effectiveness of pulmonary rehabilitation is well-established. However, access to pulmonary rehabilitation is limited. Home-based pulmonary rehabili-

tation has been shown to be an effective, equivalent alternative to outpatient pulmonary rehabilitation in COPD patients.

The opportunity to offer different pulmonary rehabilitation settings tailored to individual needs should improve accessibility to this intervention.

Sustained long-term physical activity remains the most important challenge for COPD patients. We need a dependable system of coordinated health care interventions and communication, and components that include self-management support.

Self-management should be an integrated part of pulmonary rehabilitation and remain long after the pulmonary rehabilitation is completed.

By early identification of patients who may have difficulty maintaining exercise and implementing appropriate self-management interventions during and after the rehabilitation program, it may be possible to promote better long-term involvement in physical activity.

Pulmonary rehabilitation should not stand alone; the best program is that which can be maintained to translate into a continuous increase in the activities of daily living.

Future research should evaluate the effect of self-management interventions combined with pulmonary rehabilitation to improve long-term activity and exercise maintenance.

INTERESTING RESEARCH

Optimizing pulmonary rehabilitation in chronic obstructive pulmonary disease - practical issues: A Canadian Thoracic Society Clinical Practice Guideline.

Marciniuk D, Brooks D, Butcher S, Debigare R, Dechman G, Ford G, Pepin V, Reid D, Sheel A, Stickland M, Todd D, Walker S, Aaron S, Balter M, Bourbeau J, Hernandez P, Maltais F, O'Donnell D, Bleakney D, Carlin B, Goldstein R, Muthuri S; The Canadian Thoracic Society COPD Committee Expert Working Group.

Canadian Respiratory Journal, 2010 July/August; 17 (4):159-168.

Abstract

Pulmonary rehabilitation (PR) participation is the standard of care for patients with COPD who remain symptomatic despite bronchodilator therapies. However, there are questions about specific aspects of PR programming including optimal site of rehabilitation delivery, components of rehabilitation programming, duration of rehabilitation, target populations and timing of rehabilitation. The present document was compiled to specifically address these important clinical issues, using an evidence-based, systematic review process led by a representative interprofessional panel of experts. The evidence reveals there are no differences in major patient-related outcomes of PR between nonhospital (community or home sites) or hospital-based sites. There is strong support to recommend that COPD patients initiate PR within one

month following an acute exacerbation due to benefits of improved dyspnea, exercise tolerance and health-related quality of life relative to usual care. Moreover, the benefits of PR are evident in both men and women, and in patients with moderate, severe and very severe COPD. The current review also suggests that longer PR programs, beyond six to eight weeks duration, be provided for COPD patients, and that while aerobic training is the foundation of PR, endurance and functional ability may be further improved with both aerobic and resistance training.

Wood Smoke Exposure and Gene Promoter Methylation are Associated with Increased Risk for COPD in Smokers.

Akshay Sood, Hans Petersen, Christopher M Blanchette, Paula Meek, Maria A Picchi, Steven A Belinsky, and Yohannes Tesfaigzi; University of New Mexico, Lovelace Respiratory Research Institute, University of Colorado at Denver, United States.

American Journal of Respiratory and Critical Care Medicine, 2010, doi:10.1164/rccm.201002-0222OC

Rationale: Wood smoke-associated COPD is common in women in developing countries but has not been adequately described in developed countries.

Objectives: To determine whether wood smoke exposure was a risk factor for COPD in a population of smokers in the United States.

Methods: For this cross

sectional study 1,827 subjects were drawn from the Lovelace Smokersâ€™ Cohort, a predominantly female cohort of smokers. Wood smoke exposure was self-reported. Post-bronchodilator spirometry was obtained and COPD outcomes studied included percent predicted FEV1, airflow obstruction, and chronic bronchitis. Effect modification of wood smoke exposure with current cigarette smoke, ethnicity, sex, and promoter methylation of lung cancer-related genes in sputum on COPD outcomes were separately explored. Multivariable logistic and poisson regression models were used for binary and rate-based outcomes, respectively.

Measurements and Main Results:

Self-reported wood smoke exposure was independently associated with lower percent predicted FEV1 (point estimate - 0.03 ± 0.01 {S.E.}) and higher prevalence of airflow obstruction and chronic bronchitis (ORs 1.96 {95% C.I. 1.52, 2.52} and 1.64 {95% C.I. 1.31, 2.06} respectively). These associations were stronger among current cigarette smokers, non-Hispanic whites, and men. Furthermore, wood smoke exposure interacted in a multiplicative manner with aberrant promoter methylation of the p16 or GATA4 genes on lower percent predicted FEV1.

Conclusions: These studies identify a novel link between wood smoke exposure and gene promoter methylation that synergistically increases the risk for reduced lung function in cigarette smokers.

If you know of any research, articles or other publications that would be of interest to our readers please contact us.

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Visit us on the web
at
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Our website is continuously updated with useful information for Alphas, their caregivers and healthcare providers, as well as news on promising research. Make a habit of checking our website regularly so you won't miss out on exciting updates and always read our monthly newsletter from top to bottom.

Help us spread awareness by sharing this newsletter with your family and friends.

If you would like to receive this newsletter by e-mail, please contact us at 1-888-669-4583 or vanessa.mclaughlin@alpha1canada.ca

This newsletter is designed to support, not replace, the relationship that exists between you and your physician. It is not the intention of this newsletter to provide specific medical advice but rather to provide the Canadian Alpha-1 Community with information to better understand their health and their diagnosed disorder.

Specific medical advice will not be provided and Alpha-1 Canada urges you to consult with a qualified physician for diagnosis and for answers to your personal questions.

Alpha-1 Canada
Making a difference in the lives of Alphas

New class of treatment for COPD may be available in Canada soon

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According to Nycomed Canada, "market authorization has not yet been obtained from Health Canada." Nycomed filed a marketing application for Daxas® (Roflumilast) with Health Canada in 2009.

Nycomed Canada Inc. is a Canadian company belonging to the Nycomed Group, a privately owned, global pharmaceutical company. Ranked by sales, the Nycomed Group is among the 30 largest pharmaceutical companies in the world.

Nycomed Canada Inc. is based in Oakville, Ontario with more than 200 employees across the country.