"Living Proof"

Patient Outcomes of Alpha-1 Antitrypsin Augmentation Therapy (Prolastin®) in Canada

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ALPHA-1 CANADA

Introduction

These treatments are critically important for those with this disease! My sister and I are living proof.

Pauline T.

This document was prepared by Alpha-1 Antitrypsin Deficiency Canada Inc. (Alpha-1 Canada). It is based on the experiences of a number of Alpha-1 Antitrypsin Deficiency patients in Canada who have been fortunate enough to receive a therapy known as alpha-1 antitrypsin augmentation therapy (Prolastin®).

Direct quotes from patients are included in red. Information in [square brackets] was added by us for clarity.

The purpose of this document is to provide information to Alberta Health and Wellness about the patient outcomes of a therapy called alpha-1 antitrypsin augmentation therapy from the patients' point of view and the outcomes experienced by those Canadians with access to this therapy.

The only brand of this therapy approved for use in Canada is called Prolastin® which is marketed by Grifols (formerly Talecris Biotherapeutics). There are also Canadians with Alpha-1 Antitrypsin Deficiency currently enrolled in clinical trials of CSL Behring's alpha-1 antitrypsin augmentation therapy product called Zemaira®. Approximately half are, of course, receiving a placebo. The experience of only one such patient (Jeanne F.) is included here.

I was asked if I wished to try a clinical drug - Zemaira, and decided I had nothing to lose, and, even if it was only a placebo, hopefully, it will help someone else!

Jeanne F.

We also understand that multi-centre clinical trials of an aerosolized version of alpha-1 antitrypsin augmentation therapy produced by Kamada, an Israeli company, are to begin shortly in Canada. There are also other brands of this therapy available outside of Canada including Aralast® and Glassia®.

The lack of equitable access to this therapy in Canada, outside of British Columbia, Manitoba and Québec or those with private coverage in a small number of plans makes it relatively easy to recruit patients in Canada who are more than willing to take the 50/50 chance of receiving this treatment versus a placebo.

Alpha-1 Canada serves many roles in the lives of Canadians affected by Alpha-1 Antitrypsin Deficiency. Two of those roles are support and advocacy. In our roles as both a support and advocacy organization for Canadians affected by Alpha-1 Antitrypsin Deficiency, Alpha-1 Canada is committed to ensuring that all Canadians affected by Alpha-1 Antitrypsin Deficiency have equitable and affordable access to all forms of treatment that may be prescribed or encouraged by their qualified medical practitioners.

We are a lay organization and registered charity. As such we cannot and do not endorse commercial products, however, if any commercial product is prescribed to anyone with Alpha-1 Antitrypsin Deficiency by a qualified medical practitioner we advocate for equitable and affordable access to it.

I am 39 years old and was recently diagnosed with alpha-1 antitrypsin deficiency when my lung collapsed in October 2009. I had previously been a very healthy woman who has never been sick; not even with a common cold.

When in the hospital, the doctors said my lungs looked like that of a 90year

old chronic smoker, and said my lung x-rays looked like Swiss cheese...

After my diagnosis, I spent some time trying to come to terms with the idea that my lung may collapse again or one day I may require oxygen or transplant or augmentation therapy....

I was feeling a little cheated and hopeless about my genetic make-up; there is nothing I can do to change it and to find out that the therapy would not be an option for me...I am a little scared. I do not require therapy at this point– thank goodness. But I am very frightened about my future. I am a single mother that has always worked very hard to make it on my own. I have always planned for the future – my home, my children's education, my retirement etc. Now, I am wondering what will happen to me if this disease progressively gets to the point that I need therapy. Will I use my retirement money or my son's education money? Who will help me get through this? How am I going to do this on my own? If this disease didn't make me feel alone before, I am definitely feeling alone now.

Beverly C.

Background

Alpha-1 antitrypsin (AAT), also known as alpha-1 antiprotease, is a glycoprotein made predominately in the liver and transported by the blood. Its purpose is to protect the lungs and other tissues from an enzyme called neutrophil elastase (NE). Alpha-1 Antitrypsin Deficiency, also known as alpha-1, A1AD, AATD and hereditary COPD, is an inherited genetic disorder that can affect the liver, lungs and skin. People diagnosed with alpha-1 have low levels of the protective protein alpha-1 antitrypsin. In some rare cases, they have no AAT at all. Individuals with low or no AAT are at risk for developing severe liver, lung or occasionally skin disease

Alpha-1 Antitrypsin Deficiency is not a disease, rather it is more accurately described as a condition or a disorder that increases the risk of developing disease, particularly of the lungs (COPD), the liver (fibrosis and cirrhosis) and the skin (panniculitis). In order to be classified as having Alpha-1 Antitrypsin Deficiency, an individual must inherit two abnormal alleles, one from each parent. Although they often experience lower than normal serum levels of alpha-1 antitrypsin, individuals who have one abnormal allele and one normal allele are referred to as carriers.

Alpha-1 Antitrypsin Deficiency is a rare genetic condition and owing to its symptoms being very similar to COPD and asthma is also rarely diagnosed. Statistical analyses suggest that between one in 5,000 and one in 7,000 Canadians may have this condition. Not everyone with the condition will develop disease and it is unknown how many will develop lung disease requiring augmentation therapy. It is also possible for someone with the condition to never develop disease or not develop disease serious enough to require therapy. So not only is Alpha-1 Antitrypsin Deficiency a rare condition, but patients who could benefit from alpha-1 antitrypsin augmentation therapy are a rare group among those with the condition.

The treatment at issue, Prolastin is only indicated for lung-affected adults, that is people with genetically acquired COPD. Prolastin has no benefit to patients who are affected only by the liver complications.

The authors of *Alpha1-antitrypsin deficiency: A position statement of the Canadian Thoracic Society* recommend reserving AAT replacement therapy for AAT-deficient patients with impaired FEV_1 of 35% to 50% predicted who are on

optimal medical therapy but continue to show a rapid decline in FEV_1.

So once again, among those patients with Alpha-1 Antitrypsin Deficiency that affects the lungs, an even smaller proportion would meet the CTS criteria.

Only British Columbia, Manitoba and Québec provide funding for this therapy.

Some patients are, understandably, reluctant to provide their private and personal medical information for inclusion in a submission to government.

There are private insurance plans which fund this treatment.

In my own particular case my lung capacity has gone from 140% of normal down to 70% of normal. I used to jog five kilometres every morning and I found that it was becoming difficult to do. I thought it was just naturally aging and the doctor said no, there's something wrong here and sent me to see a specialist and I kinda thought, I wonder what they're going to come up with.

And when the specialist said you have Alpha-1 Antitrypsin Deficiency and it's so rare I'm not even allowed to prescribe medicines for it. I thought, oh great, I'm one of the chosen few, I'd rather not be. I'll have to find out what this is and I did a bunch of research on it and found out what it was and I was really pleased that I was able to get these infusions prescribed because it's the only treatment for this condition.

It has arrested the deterioration in my lungs. If I hadn't had the infusions I wouldn't be able to do most of the things that I enjoy like sailing, skiing, jogging. I'd probably be able to work but I'd have to be thinking about retiring.

I'm really lucky because my wife has a gold-plated insurance policy which pays for the Prolastin infusions. A lot of people don't have that. When I turn 65, if my wife's insurance policy stops paying for this then my condition is going to start deteriorating again and that kinda worries me.

David M.

Prolastin is the only specific treatment available for lung-involved patients with Alpha-1 Antitrypsin Deficiency.

Alpha-1 antitrypsin augmentation therapy (Prolastin) replaces the missing alpha-1 antitrypsin in the patient's blood thus protecting the lungs from further damage from neutrophil elastase. This damage is permanent. Patients waiting for approval have experienced significant deterioration in their ability to breathe. Substantial amounts of their lung function have been sacrificed already. Since the Canadian Thoracic Society's position statement recommends reserving this therapy for patients with impaired FEV_1 of 35% to 50% some may even lose the opportunity for treatment regardless of the outcome of this submission.

As mentioned above, Alpha-1 Antitrypsin Deficiency is a rare condition that is often misdiagnosed as asthma or COPD. A survey commissioned by Alpha-1 Canada found that in Canada, it takes on average 9.9 years from the time symptoms appear until an accurate diagnosis is obtained for lung-involved patients. The wait for liver-affected patients is 4.5 years. Waiting this long to find out what is wrong and then being denied treatment because you can't afford it are circumstances the Canadian healthcare system was a response to, not circumstances it was designed to create.

My name is Allyson, I was diagnosed with Alpha 1, 20 years ago. I was first wrongly diagnosed with asthma, then I had a pulmonary function and the Dr. was alarmed at the severe C.O.P.D.

that showed up, so I had the blood test, sure enough it was Alpha 1. I live in British Columbia, in 1991 I started on Prolastin once a month, then it was proven that it was more effective if I had it every 2 weeks, I did that for a while, then I started on it for a weekly treatment. I am now 62 years old, and I know that without the Prolastin I don't believe I would be here.

Far too often this rare disease is misdiagnosed as asthma, if this is caught early enough the Prolastin prolongs life by keeping the lungs from getting worse. My sister also has it as well, she lives in Penticton B.C., and is also on Prolastin. I believe it would prove to be a disservice to Canadians, if this life saving medication is not available to our citizens.

Our medical system is supposed to take care of our fellow Canadians. What if it was you or one of your family members? Please consider this.

Allyson G.

Living with Alpha-1 Antitrypsin Deficiency

Physical Effects

Along with shortness of breath, the lung affected patient with Alpha-1 Antitrypsin Deficiency who is not receiving Prolastin treatment experiences many more debilitating conditions and situations that they seek to avoid or limit. We apologize in advance as the language necessary to describe some of this is not for the squeamish.

My name is Annie C., I am writing on behalf of my daughter Victoria M., she is 38 years old she has COPD, plus end stage emphysema and Alpha 1 Antitrypsin Deficiency, which affects her lungs, she is on 24 hrs oxygen, cannot walk more than a few steps, has to have help bathing, is very limited as to what she can do. She has had these health issues for many years, but the last 2 years her health has got progressively worse so much so that she could no longer live alone, with her daughter now 13 years old.

Victoria's only other option was to go into a care facility and basically wait to die, and put my granddaughter into care.

I then became the care giver and took the responsibility for both my daughter and granddaughter, I myself am 56 years old, single no other relatives who can help I live on a limited budget. I did have some savings but during the past 2 years that has since been eaten up. Victoria gets disability benefits & child support, which just pays for the basics, especially as we live in Oakville Ontario, and properties are extremely expensive. We rent as I do not have the luxury of owning my own home. We have to rent a bungalow as Victoria cannot climb stairs, we tried renting a townhouse at first as it was cheaper, but Victoria became very sick as she had to climb stairs which would take her over ½ hour to go up or down, then she fell down the stairs and broke her leg. We had to move, and pay $500 per month more for a bungalow. I tried to get funding for a chair lift for the stairs, but was told as we did not own the home, we did not qualify.

Annie C.

Emergency room visits and hospital admissions for exacerbations are frequent, unpredictable and eventualities the patient

dreads and takes great pains to avoid. There are also numerous visits to physicians and respirologists prior to going to emergency rooms. Emergency room visits cause patients to be racked with fear that that they will contract additional life threatening infections at the hospital; self-doubt that they erred in caring for themselves; worry that they may never recover; impatience to go home; and terror about another possible permanent decline in lung function.

A constant concern is excessive mucous production, "gagging on thick green goo with a repulsive odour that often becomes lodged in the bronchial tubes causing gagging and choking." Most times unexpected, when gruesome expectorating occurs it is very irritating and appalling for others to witness. There is dreadful embarrassment and using a Kleenex doesn't hide the amount which others understandably perceive as uncivilized. On a daily basis the mucous quantity may vary but the struggles are the same. There is an urgency to flee and hide and often the preference is to stay at home, in seclusion, whether in an exacerbation, or not.

Choking can occur when the mucous gets stuck or from excessive coughing or because the airways are restricted and swallowing is a problem both with liquids and solids or even just saliva. When choking occurs an ambulance is often called resulting in emergency room visits and often hospital admission.

The desire to eat is reduced, and weight loss occurs resulting in further compromise to their otherwise weak immune system. This causes a rush of uncontrollable panic, hysteria and terror in not knowing when, or if, their next breath will come. Patients are forever worried when the next choking spell will occur increasing their stress levels and the stress levels of family and friends. Their caregiver and family are always on alert, tense, and fearful of the next episode.

For some, the lung, a muscle, contracts creating intense, prolonged, sharp, "take your breath away pain." They are frequently at physicians' and specialists' appointments, and then subjected to poking, prodding, an overwhelming amount of lab tests and CT scans to rule out co-morbidities. Their uncertainty and fear is heightened, they are perplexed and plagued with self-doubt: have they developed additional complications, heart problems? Time is no longer theirs or their family's; activities are halted; increasing disappointment and increasing anger for all who care for them.

Lung infections, including pneumonia are recurring affairs. These infections are long lasting, irreversible complications. They often occur during peak infectious flu seasons or times allowing for insufficient recuperation before the next infection. Recovery takes weeks, even months of bed rest wearing their spirits down. They feel discouraged, defeated, that they have lost control of their destiny and even jealous of others' ability to breath and live life. Patients can feel humiliated and crushed by their physical weakness; saddened that others are burdened with their long term care; distraught that they've become an inattentive spouse, parent, grandparent and friend.

The lung affected patient with Alpha-1 Antitrypsin Deficiency who is not receiving Prolastin endures a daily persistent nagging cough accompanied by a painful sore irritated throat, breathlessness, sore chest, back and lung pain. There are constant bouts of exhaustion – during an exacerbation the severity doubles and triples, many times requiring hospitalization and increased supplemental oxygen. They wonder where to put themselves so as not to disturb anyone or spread germs – no place appears inviting. Even their own home becomes uncomfortable. They isolate themselves to one room or their family does. People go out of their way to avoid them. No one wants to "catch" whatever it

is they have (the infection, not Alpha-1 Antitrypsin Deficiency). They are anxious, restless, irritable and become germaphobes.

The inevitable build-up of scar tissue in the lungs which accompanies each exacerbation weighs heavy on their minds. They are devastated that once the exacerbation passes their quality of life will further deteriorate, activities will diminish and they become overwhelmed with uncertainties.

And then there is the bad news about the good news. The medications prescribed for infections and exacerbations that provide some relief have their own complications. Excessive use of antibiotics leads to a well-placed fear that someday they may simply stop working, then what?

But the most chilling fear is to be back on Prednisone. Patients on Prednisone report, "increased hypersensitivity," "difficulty sleeping," "feeling of a whirling motion," "increased or loss appetite," "increased sweating," "indigestion," "severe allergic reactions (rash; hives; itching," ironically, "difficulty breathing," "tightness in the chest," "swelling of the mouth, face, lips, or tongue) ," "black, tarry stools," "changes in menstrual cycles," "convulsions," "diarrhea," "dizziness," "fever," "general body discomfort," "headache," "increased pressure in the eye," "joint or muscle pain," "muscle weakness," "prolonged sore throat," "cold, or fever," "puffing of the face," "severe nausea or vomiting," "swelling of feet or legs," "unusual weight gain," "vomiting material that looks like coffee grounds," "weakness," "weight loss," "embarrassing, uncontrollable, fluctuating mood swings," "nervousness," "depression," "exaggerated sense of well-being or doom," "personality changes," "poor concentration," "spacing out," "unable to function at work," "on committees," "run a business or home."

When living with an incurable and progressive disease it is difficult to not consider disease progression. From further deterioration of the lungs to possible transplantation and the enormous expenses associated with pre and post-transplant care. These thoughts cause an erosion of emotional strength to fight for survival. Patients are on a constant emotional roller coaster ride. With the inevitable ups and downs comes upheaval of their routine. In time they are devastated over loss of employment, financial worry and burdensome confusion. They experience immense anger and disappointment that they are in this unenviable position because they live in the wrong province of a country without equitable access to the treatment that would have made this all so unnecessary.

Dr. Ken Chapman wrote on my behalf to the government for me to be able to get Prolastin, of course I was refused so in turn he also wrote a section 8 letter on my behalf and again I was refused. I notified my insurance company and unfortunately was not covered under my plan.

I will need my transplant within the next year or so, I am deteriorating at a fast pace now, so I just have to wait to become critical, gasp for every breath and then wait for someone to die in order for me to have a chance to live. This should be taken care of while we are strong enough to fight off infections, not when our immune system is too weak to fight.

Having the transplant is one thing coming out of it ok is another, I personally know of an Alpha 1 patient who had the transplant only to get infected lungs and to die of lung cancer. Who paid the price, the government or the patient? So no there is no guarantee so why not give us all a fighting chance.

Karen V.

Other symptoms reported include "hip fracture," "appetite change," "weight change," "digestive upsets," "unwanted flatulence," "intense discomfort," "headaches," "tension," "muscle aches," "pounding heart," "fatigue," "insomnia," "restlessness," "vivid nightmares," "accident prone," "teeth grinding," "restlessness," "foot tapping," "finger drumming," "chest tightness," "airways blocked and swollen," "breathlessness," and "sweaty palms."

Lifestyle Changes

People with Alpha-1 Antitrypsin Deficiency who are lung-affected face three types of lifestyle changes. The first are the changes that their disease make necessary. These include the inability to walk up stairs or slight inclines, the inability to take part in the activities of daily living and the activities that families and friends share and the necessity to lug supplemental oxygen wherever they go. These changes are significant for most patients and cause mental anguish as their reality sinks in.

The second are those changes forced upon them by a less than compassionate society. These changes include chastisement for high employment absenteeism, which often leads to being forced on to disability or in to early retirement. There is also the well-meaning, yet still disheartening tendency by others to "take over" many activities of daily living from carpooling to lawn care to grocery shopping to taking the children or grandchildren to the park.

Finally there are the lifestyle changes they make themselves in an attempt to preserve their failing health.

Alpha-1 Antitrypsin Deficiency patients find it necessary to make lifestyle changes to avoid deteriorating symptoms and especially exacerbations. Those who are lung-affected only must do likewise to escape or prolong the development of liver disease. Chief among these are avoiding irritation to the lungs, for example passive cigarette smoke, wood smoke, dust, fumes, chemicals, most cleaning products and other lung irritants. In order to avoid infections that may lead to exacerbations patients avoid large gatherings of people, public places, school age children, including their own children and grandchildren, and child care, healthcare or long term care facilities when not a patient.

They also refrain from drinking alcohol. The consumption of alcoholic beverages can cause damage to the liver in normal people and many authorities recommend low, infrequent or no alcohol consumption for patients with two deficient alleles, and patients with any indication of liver damage.

Although it may sound counter intuitive, despite the incredible effort required and shortness of breath experienced, exercising regularly is also important for patients to preserve lung function as is eating a well-balanced diet.

Patients must always review labels of over-the-counter medications, vitamins or herbal supplements carefully. They avoid products with acetaminophen and alcohol, both of which can injure the liver. If vitamin supplements are required, they ensure appropriate dosage of fat soluble vitamins as any overdose can accumulate in the liver. Other supplements are only taken under the advice of their physician.

Environmental Awareness

Environmental changes include avoiding pollutants that irritate the lungs, as well as avoiding liver toxins. Individuals must assess their home and work environments carefully, and consult with an occupational medicine specialist if indicated. Examples of environmental irritants are, cigarette smoke, industrial and occupational pollutants such as dust, flower and tree pollen, ash, volatile compounds, fumes

and other allergens, air pollution, wood-burning stoves, fumes from cleaning solvents such as bleach, ammonia or household and industrial cleaners, paints and/or toxic agents. Precautions are also taken when handling chemicals and other materials, as those may be absorbed through the skin. The liver detoxifies poisonous chemicals that enter the body. If the liver is damaged, the detoxification process is altered.

Increased Doctor Visits

People with Alpha-1 Antitrypsin Deficiency seek expert medical treatment frequently and visit their healthcare provider more often. Exacerbations require emergency room visits and often admission to hospital for an average of ten days.

Comorbidities

Comorbidities are common for people who are lung-affected by Alpha-1 Antitrypsin Deficiency, especially those without access to Prolastin because organ systems work differently when they do not receive enough oxygen.

Comorbidities are also difficult to manage for people who are lung-affected by Alpha-1 Antitrypsin Deficiency. Patients must pay particular attention to their health at all times, and especially when another condition occurs.

I have recently been diagnosed with this genetic illness. It is terrifying enough to deal with now I find out that augmentation therapy funding may not be available....

People with alpha-1 antitrypsin deficiency are ill through no fault of their own. It is a hereditary disease that they did not ask for.

Since alpha-1 antitrypsin deficiency is a rare disease, many doctors are unfamiliar with it and it can take years to be properly diagnosed. I always thought that waiting years to find out what is wrong with you and then not being able to afford the proper treatment is something the Canadian healthcare system was designed to prevent.

Without funding for augmentation therapy people with alpha-1 antitrypsin deficiency will live a life where it becomes more and more difficult to breathe, carry oxygen with them, which the government will pay for; visit emergency rooms and often be admitted for exacerbations, which the government will also pay for; and then if they are lucky have a lung transplant, which, again, the government will pay for. In a time of mounting deficits, why would you make a decision to save money today by creating a much larger future liability on the backs of people who are sick through no fault of their own?

MargaretAnn K.

It goes without saying that comorbidities that develop in the absence of Prolastin treatment put additional stress on the healthcare system.

Two common heart problems are pulmonary hypertension (high blood pressure in the lungs) and corpulmonale (heart failure that results from lung disease). It should be noted that the combination of lung disease and heart disease is incredibly disabling.

Osteoporosis is a condition that weakens a person's bones, which puts a person at a greater risk for falls and fractures. Some people living with COPD whether the result of Alpha-1 Antitrypsin Deficiency or not have other risk factors associated with osteoporosis including smoking, low vitamin D levels and use of steroids for

treatment (see discussion of prednisone above). Women with COPD and osteoporosis are at a greater risk for hip fractures.

Current research shows that there might be a connection between diabetes and Alpha-1 Antitrypsin Deficiency because both conditions involve inflammation. Also, some of the medications used to treat the symptoms of Alpha-1 Antitrypsin Deficiency may worsen hyperglycemia, which results in symptoms of diabetes such as blurry vision, frequent urination, thirst and hunger.

Lung Infections/Exacerbations

Although discussed at length elsewhere in this submission, people living with Alpha-1 Antitrypsin Deficiency experience frequent lung infections, including pneumonia. Again, these events place additional stress on the healthcare system by requiring emergency room visits and often hospital admission.

Other conditions that may occur with lung-involved Alpha-1 Antitrypsin Deficiency include stroke, depression, anemia, anxiety, cognitive decline, GERD, glaucoma, and sleep disorders.

Outcomes

All of the outcomes reported by patients receiving augmentation therapy that were communicated to Alpha-1 Canada were positive. These outcomes fall into seven broad categories.

- fewer lung infections/exacerbations
- less severe and shorter duration of lung infections/exacerbations
- fewer emergency department visits and admissions to hospital for lung infections/exacerbations
- slowed decline in forced expiratory volume in the first second (FEV_1)
- increased energy levels, mobility and independence
- increase in the ability to take part in family activities and activities of daily living
- reduced anxiety about being a burden on family, friends and the medical system
- the ability to continue working, less disability and a limited return to work

It should also be noted here that in general people with COPD, including those whose COPD is related to Alpha-1 Antitrypsin Deficiency, experience a significant decrease in their overall level of lifetime earnings, and face a future of financial uncertainty (Fletcher, Monica J. et. al., COPD Uncovered: An International survey on the impact of chronic obstructive pulmonary disease (COPD) on a working age population, BMC Public Health 2011, 11:612). This study also found that,

- COPD patients lose an average of approximately US$1,800 of their income each year as a direct result of their condition, equating to an estimated lifetime loss of nearly US$20,000 per individual.
- In addition, nearly 1 in 5 of 45-67 year olds with COPD are forced to retire prematurely due to the condition, thereby incurring increased healthcare utilisation costs, reducing their personal tax and pension contributions and increasing disability allowance costs to governments
- People with COPD feel unable to confidently plan for the future. The impact of COPD on a patient's earning power and overall household income makes them concerned about its future impact on their lives, and those of their family, and their ability to maintain the same lifestyle as they had before

Patients not receiving Prolastin have also

reported to us of being "forced" into early retirement or onto long term disability due to frequently taking sick time.

For most of the last 50 years I have been a distance runner. Some of the time I have been moderately competitive within my age group. For instance at age 16 I could do a mile in less than 5 minutes; at 40, ten kilometers under 40 minutes; at 45, marathons in less than 4 hours.

Ironically, physical fitness both hindered and helped the diagnosis of Alpha 1. It hindered because for about 13 years my doctor kept telling me that declining performance was just due to aging and I was still faster than 95 percent of my peers anyway. It helped in that a perceptive holistic chiropractor finally recognized abnormal shortness of breath and suggested that I insist on a referral to a respirologist.

The diagnosis was hard-hitting. It required a painful psychological adjustment to recognize that no matter how hard I trained, I would never again be a fast distance runner. But I kept running — slower, of course, and shorter distances. I also concentrated more on other aspects of fitness like upper body strength which requires less aerobic effort. I wanted to maintain what fitness I could.

Slowly I began to realize that I could still experience the thrill of speed over a very short distance. So I began to train for short dashes. They don't require the same aerobic capacity. They are finished before the oxygen deficit overcomes me.

Now I am 63 years old. I had never been in a formal 100 meter dash in my life. But the Masters Track and Field competition was scheduled in June. Why not try it?

The result amazed me! I did the 100 meters in 15.5 seconds which earned the bronze medal in my age group. The silver medal time was 15.0; gold was 13.8; fourth place was 20.61 and fifth was 21.21.

Is it hard? It sure is. I am still gasping and hardly able to walk when competitors have long ago recovered their breath. Sometimes during intense training the body panics and tells me that I am about to die in oxygen deficit because I will never catch my breath. But in the mind I have to reassure myself that I will recover and not die from this.

What's the future? Do I have potential for improvement after that first race or is it all downhill from here? I don't know. But I hope to have fun finding out. I still have a higher than predicted FVC (6.60) and a mediocre FEV_1 (2.36). I am on Prolastin, so further lung function deterioration should be moderate.

Syl G.

Living with the lung disease associated with Alpha-1 Antitrypsin Deficiency means constant difficulty breathing. Patients describe the sensation as feeling as though they are breathing through a straw or like someone is sitting on their chest. Excessive mucus production must be regularly cleared, which is exhausting and embarrassing. They experience shortness of breath from simple tasks of daily living such as showering or climbing stairs. Emergency room visits, with associated wait times and frequent hospital admissions.

Exacerbations

Respiratory infections are the most common cause of exacerbations also known as flare-ups.

The specific viruses responsible for exacerbations are often influenza, rhinovirus, or adenovirus. Recent evidence suggests exacerbations are often caused by certain kinds of bacteria known as mycoplasma and chlamydia type organisms. Other bacteria commonly associated with exacerbations are Streptococcus pneumoniae (pneumococcus), Hemophilusinfluenzae, and Moraxella catarrhalis.

Bacteria, viruses and fungi can cause infections in various parts of the lung, leading to bronchitis, bronchiolitis, and pneumonitis or pneumonia.

According to a Canadian article published in 2008 (Mittmann, N. et al. 2008, The cost of moderate and severe COPD exacerbations to the Canadian healthcare system, Respiratory Medicine 102, pp. 413-421) hospital admissions for COPD exacerbations averaged a 10-day length of stay at a cost of $10,000 per stay. The same article conservatively estimated the total cost of COPD hospitalizations at $1.5 billion a year. And yet another article published by Mittman et al. states that the simplest way to reduce hospital admissions for COPD is to prevent exacerbations by treating the disease appropriately.

Exacerbations are not just a symptom of COPD; they actually cause the disease to progress, points out Dr. Jean Bourbeau, Director of the Respiratory Epidemiology and Clinical Research Unit at the Montreal Chest Institute. "These attacks cause lasting damage — the patient's lung function will never be the same again."

The way to prevent further damage to the lungs is to treat the underlying illness, "We have to treat the acute event then initiate long-term COPD treatment to prevent further attacks,"Bourbeau says.

Patients receiving Prolastin infusions all report fewer exacerbations and a significant number report no further exacerbations at all. Those exacerbations experienced are less severe and of a shorter duration.

For example, Pauline T. who has been receiving Prolastin therapy for 14 years says that, "Other than the typical inhalers (Symbicort, Ventolin, and Spiriva) there has been no other medical intervention."

Syl G., a competitive runner who switched from marathons to 100 metre dashes after his diagnosis, told us that, "I have had no lung infections at all since I started on Prolastin."

Rick K. on the other hand reports that, "the number of infections decreased as did the length of time it took to get over them, the overall physical effects of the infections were lessened substantially." [on Prolastin].

Jeannine F. Has "not been sick for a long time."

An exacerbation is a sustained worsening of the patient's condition from the stable state and beyond normal day-to-day variations, necessitating a change in regular medication.

The patient must be ever vigilant to recognize when symptoms are changing. Treatment must begin promptly to reduce permanent lung damage. Many physicians will prescribe medications for exacerbations in advance so that the patient can begin treatment immediately when an exacerbation begins.

All patients with Alpha-1 COPD have an increase in cough, sputum production, and breathlessness. Being able to tell a "bad day" from a more prolonged exacerbation is important, and is difficult to do. Some factors that may cause a bad day include: weather, allergies, barometric pressure changes, higher altitude, emotional variability and using an empty or dysfunctional inhaler.

Early symptoms or warning signs of an exacerbation are unique to each patient. Usually the patient will be the best person to know if they are experiencing an exacerbation. The most common signs and symptoms associated with an exacerbation are: worsening of a previously stable condition; increased difficulty breathing, even at rest; increased wheezing; increased coughing; increased amount of sputum production; a change in the characteristics of sputum, such as appearing to be more thick/sticky, or a change in color from clear or white to yellowish-green, or the presence of blood in the sputum; chest tightness; irritability and/or change in personality; fluid retention (swelling in the hands or feet); forgetfulness; confusion; slurring of speech; and sleepiness.

Typically, an exacerbation is accompanied by: increased levels of fatigue, a prolonged period of lack of energy; requiring more pillows to sleep or sleeping in a chair instead of a bed to avoid shortness of breath; fever; rapid breathing; skin tone changes to "ashen" or "blue" colour, known as cyanosis, especially seen in the fingertips and/or lips; increasing morning headaches; dizzy spells; restlessness; and rapid heart rate.

Medications for the treatment of exacerbations also take a toll on the patient. Medications include short-acting beta2-agonists, bronchodilators, long-acting bronchodilators, inhaled steroids, antibiotics, expectorants and oral steroid administration, typically Prednisone. Once improvement occurs the patient must be weaned off Prednisone over 10 days to two weeks to a low daily or alternate-day dosing and then changed to an inhaled steroid.

Although outlined in more detail above, the potential short-term side-effects of regular use of Prednisone include: hip fracture, insomnia; mood changes; personality changes; euphoria; psychotic behaviour, or severe depression, it may even worsen any existing emotional instability in some individuals. At a high dosage, Prednisone may cause high blood pressure and fluid retention. With prolonged Prednisone treatment, eye problems may develop (e.g. a viral or fungal eye infection, cataracts, or glaucoma).

Additionally, if Prednisone is taken over the long term, the build-up of adrenal hormones in the patient's body may cause a condition called Cushing's syndrome. This condition is marked by weight gain, a "moon-faced" appearance, fragile-thin skin, muscle weakness, brittle bones, and purplish stripe marks on the skin.

Given the symptoms of an exacerbation, it is perhaps stating the obvious to say that during such an event the activities of daily living take a backseat to bed rest and all of a patient's energies are devoted to taking the next breath. The Lung Association may have said it best, "when you can't breathe, nothing else matters."

Patients receiving Prolastin report that the number of exacerbations they experience on Prolastin as compared to before their treatment began can decrease from as many once a month to as few as two or three per year. A very significant number of patients report no further exacerbations at all.

Additionally, those who do continue to experience infrequent exacerbations report that the exacerbations they do experience are less severe and last only a few days compared to longer than one week. Exacerbations experienced by the patients we have spoken to who are on Prolastin almost never require an emergency room visit or hospitalization. Patients not on Prolastin report frequent emergency room visits and hospitalizations.

When I turned forty that's when the trouble started. I was sick all the time with pneumonia. I would finally get over being sick then pneumonia would set in again. I was eventually put on

prednisone which allowed my bronchial tubes to open. This drug however, had numerous side effects including, weight gain, bone loss, diabetes and many others.

This went on for almost two decades and that's when I was introduced to Prolastin 3 years ago. I have not been sick for a long time. I feel that this is the greatest drug and my health has changed for the better. I can finally go shopping, clean the house along with many other daily activities. This drug has also allowed me to get back to my family because I feel so much better. My family is the most important thing to me and after raising 3 daughters of my own I can now enjoy the time spent with them and my nine grandchildren.

Instead of taking care of me all the time my husband and 3 daughters can now enjoy me because I feel like I have my life back again.

Jeannine F.

Slower decline in FEV_1

Patients receiving Prolastin are monitored closely by their physicians and keep a close eye on their FEV_1. FEV_1 stands for Forced Expiratory Volume in the first second and is measured using spirometry.

FEV_1 is the volume of air that a patient can forcefully blow out during the first second of the FVC. A decrease of the FEV_1 compared to normal values (obtained from non-smoking, normal subjects of the same age, height and sex), may indicate a slowing of air flow rates. Chronic obstructive pulmonary diseases (COPD) such as emphysema (including emphysema associated with Alpha-1 Antitrypsin Deficiency), asthma, or chronic bronchitis can reduce flow rates.

It is important to note that everyone's lung function decreases with age. Sadly, for patients with Alpha-1 Antitrypsin Deficiency this decline occurs at a much faster rate due to the lack of circulating alpha-1 antitrypsin in their blood stream. A patient with Alpha-1 Antitrypsin Deficiency would be doing very well indeed if double digit decreases in their FEV_1 were reduced to single digit decreases, and this is an outcome people receiving Prolastin report.

Given that FEV_1 is reported as a percentage of "predicted" or normal and the predicted decreases with age, most patients that we have spoken with report a "levelling off" of their FEV_1 decline after beginning treatment with Prolastin. In other words, the decline becomes normal.

Daryll S. told us that, "My doctor in Edmonton has all the info on this and we both look at these numbers and show that Prolastin does slow down the progression of the disease."

Kim I. reports that, "I have been receiving Prolastin for the past 4 years and I know by my quarterly test results the reason I am not progressing at the speed before the bi-monthly treatments is because of this life saving drug."

Pauline T. states that "As evidence of the stabilizing nature of the treatments I note that my pulmonary function test results have been largely stable since I began the program [Prolastin]."

Rick K. notes that, "My FEV_1 dropped about 1% in each of the first couple of years [of treatment], and then I levelled out."

Improved Quality of Life

Patients receiving Prolastin report increased energy levels; increases in the ability to take part in family activities and activities of daily living; and the ability to continue working or less disability and a limited return to work. These outcomes have been grouped together as

improvements in quality of life.

Almost immediately, my energy level increased, the number of infections decreased as did the length of time it took to get over them, the overall physical effects of the infections were lessened substantially. My FEV_1 dropped about 1% in each of the first couple of years, and then I levelled out.

Rick K.

I'm no longer working. But I did work. I worked for thirty years with the social service department and I went for Prolastin therapy treatments every two weeks for twenty years of that thirty and I wouldn't have been able to do that, I wouldn't have been able to care for the community and do the things I did without those bi-weekly infusions. Since September of 2010 I've been on weekly infusions and that has been very promising for me as well. I wouldn't be here if it hadn't been for that medicine – I know that...

Eileen A.

Patients report a wide range of outcomes. Syl G. a former marathon runner was able to take up short distance running at a competitive level. Rick K. can now supplement his disability income with occasional work, cutting his own grass and doing chores around the house. Jeannine F. can now go shopping, clean the house, perform other daily activities and get back to her family because she feels so much better. And at 58 years old, Pauline T. believes that, "if I were not taking the infusions I would be not doing as well as I am – I may not even have survived this long."

Since beginning Prolastin, although I have never been able to go back to work fulltime, I have been able to supplement my disability to the allowable limit, with occasional work here and there. I am still able to cut my own grass, and I still do lots of chores around the house. My quality of life is certainly much improved than before I began my treatments. My doctors are amazed that after 21 years of living with Alpha 1, I continue to maintain relatively good health and a fairly good saturation level given my current FEV_1 of 35%.

Rick K.

After 18 years of Prolastin infusions, Jack K. died at the age of 81 from a fall and ensuing head injury.

Eileen A. is perhaps the Canadian patient who has received Prolastin for the longest time, over 20 years. Her treatments have been funded by her private healthcare insurance over all of that time. She continued to work at her career in social services and be an active member of her community for fifteen additional years before finally accepting a disability pension at the age of 58. Although no longer working, Eileen says, "I continue to do all the things I love. I love to paint. I love to garden. I love to be on vacation and I certainly love to be with my grandchildren. I believe that without Prolastin I wouldn't be here talking about this."

Conclusions

The outcomes experienced by patients receiving Prolastin in Canada over the last 20 years overwhelming prove that Prolastin is a safe and effective treatment for those who meet the guidelines for use as set out by the Canadian Thoracic Society.

Patients experience

- fewer lung infections/exacerbations

- less severe and shorter duration of lung infections/exacerbations
- fewer emergency department visits and admissions to hospital for lung infections/exacerbations
- slowed decline in forced expiratory volume in the first second (FEV_1)
- increased energy levels, mobility and independence
- increase in the ability to take part in family activities and activities of daily living
- reduced anxiety about being a burden on family, friends and the medical system
- the ability to continue working, less disability and a limited return to work

It would be an incredible disservice to patients and their families, as well as to the other parts of the healthcare system which will deal with the treatment of symptoms and comorbidities, to not fund this lifesaving treatment immediately.

This evidence forms clear and definitive reasons for funding of Prolastin. Indeed, as the title of this document suggests, the patients who contributed to this document are the "living proof" that the Alberta Health and Wellness must base its decision on.