Patient Information Handbook

Published by the
Pulmonary Fibrosis Foundation
as a public service to the Pulmonary Fibrosis Patient Community

"Pulmonary Fibrosis...it takes your breath away"

There is no cost to the patient for this handbook but donations will be gladly accepted to help defray the cost of publication. Send your contribution to the Pulmonary Fibrosis Foundation at 1332 N. Halsted Street, Suite 201, Chicago, IL 60622 312.587.9272

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Acknowledgments

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We extend our appreciation to the staff of the Foundation for all the long hours and dedication devoted to the preparation of this handbook. In addition we would like to thank the members of our Scientific and Medical Advisory Board for reviewing this booklet for medical and scientific accuracy. Finally, we wish to thank all the well wishers for their encouragement and kind words regarding the content and importance of this endeavor.

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Introduction

Patients often call the Foundation with the news they have just been diagnosed with Pulmonary Fibrosis, feeling frightened, confused and concerned. Family and friends of patients with Pulmonary Fibrosis also call, struggling to understand how they can support their loved ones. The Foundation created this booklet to provide knowledge, understanding and hope for those afflicted with Pulmonary Fibrosis. By offering this information, patients and their family or friends can become more familiar with the effects of the disease and bring hope at a time when the road ahead appears to be paved with obstacles.

The information in this handbook is intended as a brief overview of Pulmonary Fibrosis and is for educational purposes only. It is not intended to be a substitute for professional medical advice. Always consult your own physician or healthcare provider with any questions you may have regarding your specific medical condition. Please know that you can contact the Pulmonary Fibrosis Foundation with any questions or comments. Call 312.587.9272 or email: breathe@pulmonaryfibrosis.org

"*Most of the important things in the world have been accomplished by people who have kept on trying when there seemed to be no hope at all.*"-Dale Carnegie

"*What oxygen is to the lungs, such is hope to the meaning of life."*- Emil Brunner

"*Resolve to live as with all your might while you do live, and as you shall wish you had done ten thousand years hence*."
- Jonathan Edwards

The handbook has been published by the Pulmonary Fibrosis Foundation to help the hundreds of thousands of patients diagnosed with Pulmonary Fibrosis understand and cope with being stricken by this often terminal illness.

Most patients find themselves totally frustrated by the lack of information forthcoming from their physician. Rarely does the doctor take the necessary time to explain to his patient all the details of the disease or help the patient deal with the trauma of being told that he/she has an illness for which there is no cure.

We hope that reading this book will provide the necessary insights to make those choices and adjustments that will improve your quality of life and help you develop a more positive approach and a realistic view of the future you face. Research has shown that an individual's mental attitude can add to or detract from their longevity.

We can look to our future as a challenge to be overcome or give in to despair. As a victim of this disease, I choose to devote my remaining days to being part of the fight to find a cure, secure in the knowledge that this will be achieved. The how and the when will be determined by the medical and scientific communities. What we can do is provide them with the assistance and encouragement that will speed that progress. All of us can participate in this common struggle. Please join us so that the day of victory will come sooner.

Michael Rosenzweig, Ph. D.
President
Pulmonary Fibrosis Foundation
1332 N. Halsted St. Suite 201
Chicago, Illinois 60622-2691
312.587.9272

Chapter One

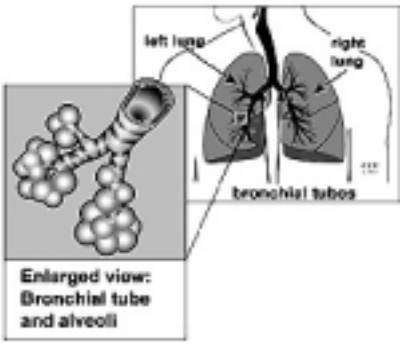
Understanding Pulmonary Fibrosis

The Lungs

To understand this disease, it is important to know how normal lungs are built and how they work. This will help you comprehend what happens to the lungs, why people have certain symptoms, and what the patient and the doctor can do to decrease breathlessness.

The body's functions depend upon a steady supply of oxygen. Unfortunately, the body cannot store oxygen so the supply must be fresh and continuous. In addition, waste products such as carbon dioxide must be excreted promptly. If carbon dioxide builds up in the body, it creates an imbalance of acids in the blood. In excess these acids can impair brain and heart functions and cause such symptoms as headache, drowsiness and fatigue.

The lungs are responsible for the exchange of gases. Oxygen goes in, carbon dioxide comes out. Here is how it works. The airways of the lungs look like an upside down tree. The biggest branch is the trachea or windpipe. It branches into smaller bronchial tubes. The very smallest branches are called bronchioles which branch into a cluster of little air sacks called alveoli.



There are about 300 million alveoli in the lungs. Each of these air sacs is surrounded by tiny blood vessels called capillaries. This is where the gas exchange takes place.

Fibrosis or scarring begins in the interstitium. The interstitium is the tissue between the air sacs. Imagine a tub filled with balloons. The balloons are the alveoli, or air sacs. Where the balloons touch each other represents the interstitium. Normally, this is a thin tissue layer with just a few cells in it. When scarring occurs the tissue becomes thicker and the lung becomes stiff, making it more difficult for oxygen to get into the bloodstream.

While there are many lung diseases that lead to shortness of breath (dyspnea), they generally fall into two main categories: obstructive diseases or restrictive diseases.

Obstructive lung diseases are *airflow* problems. Air can get in but gets trapped and has trouble getting out. Things that limit or obstruct the flow of air include constriction or narrowing of the breathing tubes, increased secretions and swelling of the lining due to inflammation. Cystic Fibrosis, Asthma, Bronchitis, Emphysema and COPD are obstructive diseases.

In contrast, restrictive disease is a *low-air-volume* disorder. Not enough air can get *into* the blood stream due to thickened walls of the air sacs (alveoli). Various Pneumonias and Pulmonary Fibrosis are restrictive diseases.

Chapter Two

What is Pulmonary Fibrosis?

Pulmonary Fibrosis (PF) literally means lung (pulmonary) scarring (fibrosis). The lung scarring occurs in the tissue of the lung called the interstitium, which supports the structures of the lung (air sacs/ alveoli). There are an estimated 130-200 related diseases called Interstitial Lung Disease (ILD), that are similar in characteristics to PF and can result in scarring. PF causes the lung tissue to thicken and become stiff. Scarring inhibits oxygen from entering the blood stream.

The course of PF varies from person to person. For some, the disease may progress slowly and gradually over years, while for others it may progress rapidly. Some people may notice symptoms ranging from moderate to severe. Other people stabilize for a period of time.

Searching for information about this disease can be quite perplexing due to the many terms used to describe Pulmonary Fibrosis. For example, there are many known causes of PF, but when the cause is unknown it is called "idiopathic, " or Idiopathic Pulmonary Fibrosis (IPF). The regions of the fibrotic areas vary from case to case. They affect each person differently and at varying rates.

To make matters more complicated, IPF has *several* names, such as Cryptogenic Fibrosing Alveolitis (CFA) and Usual Interstitial Pneumonitis (UIP). The term "usual" was used in the 1960's to describe the "usual" pattern seen for the interstitial pneumonias. Fortunately, the terminology and classification has undergone modification.

In 1999, an international panel of experts released a consensus statement to provide physicians with practical, up-to-date guidelines for the treatment of Idiopathic Pulmonary Fibrosis (IPF). The consensus statement was the first instance of an attempt to codify both the causes and treatment of Pulmonary Fibrosis. Unfortunately, much of the data presented in this document is no longer current and has been replaced by newer research which challenges many of the premises presented in the statement.

There are additional lung-related diseases. Some of these include:

- Desquamative Interstitial Lung Disease (DIP). This is relatively rare, affecting twice as many men as women with an average onset age of 42 years. 90% of those affected have a history of smoking. Remission occurs in approximately 20% of patients with smoking cessation. 75% will respond to corticosteroids and complete recovery is possible.
- Respiratory Bronchiolitis Interstitial Lung Disease (RBILB). This is believed to be the same but lesser form of DIP. Average onset age is 36 years. Every person affected is a smoker.
- Lymphangioleiomyomatosis (LAM). This is a rare disease that affects only women with an average onset age of 34 years. There are about 800 cases in the United States.
- Acute Interstitial Pneumonia (AIP). This is an acute form of the disease with an abrupt onset and rapid progression to severe shortness of breath and respiratory failure. Many succumb to the disease in 1-2 months.
- Nonspecific Interstitial Pneumonia (NSIP). This is the second most common form of fibrosis, and is slightly more common in women than men with average onset at 49 years. NSIP is characterized more by inflammation than fibrosis and responds favorably to corticosteroids.

Chapter Three

What are the causes of Pulmonary Fibrosis ?

In the past, the predominant theory was that the process began with inflammation, which resulted in scar formation. However, it has recently been proposed that fibrosis itself, representing abnormal wound repair, is the primary process rather than inflammation. The process is one of gradual replacement of the lung tissue with fibrosis or scarring, resulting from some type of microscopic injury to the lung. Recent studies have shown that genetics may play a crucial role in the development of Pulmonary Fibrosis. It was previously thought that genetics was responsible for only 10% of patients with Pulmonary Fibrosis. However, the latest research reports that this number may be as high as 40%.

Fibrosis or scarring sometimes can be linked to particular causes such as prolonged exposure to occupational or environmental contaminants or dusts. This can be due to inorganic dusts such as Talc, asbestos, silica, beryllium and hard metal dusts or organic dusts such as such as bacteria and animal proteins. Some related diseases include asbestosis and silicosis. These diseases are often named after the occupations with which they are associated:

- Grain handler's lung
- Farmer's lung
- Mushroom worker's lung
- Bagassosis - Sugar Cane Workers
- Detergent worker's lung
- Maple bark stripper's lung
- Malt worker's lung
- Paprika splitter's lung
- Bird breeder's lung

An additional disease called Hypersensitivity Pneumonitis (or allergic alveolitis) is an allergic disorder caused by the inhalation of organic dusts. In some instances, an acute toxic reaction may occur at the time of exposure to a large dose of spores from a microbe, or within days, weeks or a few months. The acute reaction is generally in the form of bronchitis or asthma. In most cases, a long cumulative exposure of moderate to high levels of the contaminant is necessary over several years (10-20 years) for Pulmonary Fibrosis to develop.

Pulmonary Fibrosis has been associated with autoimmune diseases such as Rheumatoid Arthritis, Scleroderma or Lupus. In addition, lung scarring may be related to upper respiratory infections. Pneumonia and Tuberculosis are examples.

It also has been caused by drugs or certain treatments, such as antibiotics (Nitrofurantoin, Sulfasalazine), antiarrythmics (Amiodarone, Propranolol), anticonvulsants (Phenytoin), chemotherapeutic agents (Methotrexate, Bleomycin, Oxaliplatin, Erbital) and therapeutic radiation.

Chapter Four

Prevalence of Idiopathic Pulmonary Fibrosis (IPF)

IPF is much more common disease than previously thought. Below is a summary of the prevalence of the disease:

- The actual incidence is unknown.
- It is estimated that 50,000 new cases are diagnosed annually.
- More than 200,000 people in the United States suffer from this disease.
- There are at least 5,000,000 cases world wide.
- It affects both men and women, with a higher incidence in men.
- The average onset age is 40-60 but the disease can occur at any age.
- Although not as common, IPF does occur in children and as young as 3 years of age. Interstitial Lung Disease has been diagnosed in children less than one year of age.
- At least forty thousand individuals die from this disease each year.
- The number of new cases of Pulmonary Fibrosis has dramatically increased in recent years. This is primarily due to improved diagnostic procedures. In addition, air quality has deteriorated in many sections of our country and unless stringent measures are taken the situation will worsen.
- IPF has no specific geographical distribution; it is found in equal proportions in urban and rural environments. A history of smoking has been associated with an increased risk of Idiopathic Pulmonary Fibrosis. Second hand smoke has been found to pose an even greater risk.

Chapter Five

What are the Symptoms of IPF?

Symptoms aren't always present at the onset of the disease. Scarring may occur long before any symptoms develop. The main symptom is dyspnea or shortness of breath. Many patients describe it as a feeling of "breathlessness." These indications may not present themselves until the diseases has progressed substantially.

Patients often ignore the occasional difficulty with breathing, attributing it to just "getting older" or "being out of shape." As the condition progresses and the damage to the lung becomes more severe, breathlessness may occur with minor physical activity such as showering, getting dressed, speaking on the phone and eating become more difficult and sometimes nearly impossible.

Other indications include a dry hacking cough. Some people notice flu-like feelings such as fatigue, weight loss and aching muscles and joints. The patient may also become less able to fight infection. In addition, they may experience frequent tiredness, enlargement and bulb-like development of the fingertips and nails (a condition called clubbing, which exists in less than 50% of the cases).

The disease varies from person to person. For some, the disease progresses slowly and gradually over months or years while for others there is a rapid progression. In other cases it may stabilize for a period of time. The course is generally unpredictable.

Chapter Six

How IPF is diagnosed?

In many cases the family doctor/internist may misdiagnose the illness and lung specialist (pulmonologist) should be seen to properly diagnose and evaluate the illness. Very often the patient is diagnosed as having bronchitis, asthma. emphysema or pneumonia. This leads to improper medications which are of no benefit to the patient. Consequently, it is extremely important to be seen by a Pulmonologist that specializes in Pulmonary Fibrosis.

History and physical exam

The physician will hear 'crackles' or Velcro-like sounds with the stethoscope. These sounds are 'opening' sounds made by the small airways during inspiration. About 50% of patients with IPF may have "clubbing" of the fingertips. This is a widening of the fingertips due to a lack of oxygen in the blood. This is not specific to IPF and occurs in other lung disorders, heart disease and can also be present from birth.

Chest X-Ray

A routine chest x-ray may be used as a screening test. However, 5-15% of patients with significant scarring will show a normal chest x-ray.

HRCT (CT-SCAN)

High Resolution Computerized Tomography provides sharper and more detailed images than routine chest x-rays.

- "Honeycombing" suggests extensive lung scarring with destruction of the air sacs.
- "Ground-glass opacity" refers to the hazy appearance associated with inflammation.

Pulmonary Function Tests

These are breathing tests that measure the lungs' ability to exchange oxygen and carbon dioxide properly. These tests are usually done in a hospital or clinical laboratory and consist of breathing into a spirometer, and are sometimes done in a "body box" which looks like a glass telephone booth. There are three important components to a Pulmonary Function Test: 1. Spirometry, which determines how well the lungs receive, hold and utilize air; 2. lung volumes, and 3. diffusion capacity, which measures the ability of oxygen to diffuse into the blood stream.

Oximetry

This is a screening test which estimates the amount of oxygen available in the blood. A device is placed on the finger or earlobe. The oximeter transmits light at different wavelengths through small blood vessels. Normal ranges are 95-100% on room air. Oximetry does not measure carbon dioxide levels so a blood gas level measurement may be necessary in some patients.

Arterial Blood Gas

Another method of measuring blood oxygen is by direct analysis of arterial blood, usually obtained from an artery in the wrist. Because arteries contain blood that has just come from the lungs, this provides an accurate measurement of the balance between oxygen and carbon dioxide in the blood.

Bronchoscopy

This involves an examination of the bronchi, or the main airways of the lungs, through the use of a small, flexible tube called a bronchoscope. Bronchoscopy helps to evaluate lung problems or blockages and provides a means to sample tissue or fluids. Unfortunately, the lung tissue samples obtained through bronchoscopy are small and may be inadequate for definitive diagnoses.

Bronchoalveolar lavage (BAL)

BAL is done through the bronchoscope and is a way to remove a tiny sampling of cells from the lower respiratory tract. A very small amount of saline is injected through the bronchoscope and withdrawn, taking with it a tiny sampling of cells from the lower respiratory tract.

Lung Biopsy

Lung biopsy is the most revealing diagnostic step in the evaluation of patients suspected of having Pulmonary Fibrosis. This procedure is highly invasive with many risk factors that should be evaluated and may not be recommended for all individuals. Recent studies have concluded that lung biopsy should only be used if there is uncertainty about the diagnosis of Pulmonary Fibrosis and not as a routine procedure.

Exercise testing

Exercise testing is used to measure how well the lungs respond to physical activity. The methods used for exercise testing vary from hospital to hospital, but usually include the use of a stationary bike or treadmill. Blood pressure, EKG and blood oxygen levels (recorded by an electronic device placed on the ear or finger) are monitored during exercise.

Chapter Seven

How is IPF Treated?

Once scar tissue has formed in the lung, it cannot be removed surgically or with medication. Specific treatment will be determined by your physician based on:

- Age, overall health and medical history. Other medical problems that coexist may complicate treatment options.
- Extent of the disease. Because the symptoms often start slowly and progress over a period of time, the disease may be more advanced when diagnosed.
- Your tolerance for specific medications, procedures, or therapies.
- Before taking any medications, its side effects should be discussed with the Pulmonologist.
- At this time the FDA has not approved of any medication for the treatment of pulmonary Fibrosis.

In 1999, the American Thoracic Society recommended treatment, after evidence of impairment, with a combination of corticosteroids and cytoxic agents such as cyclophoshamide or azathioprine. This course of treatment has not proven to be effective for most patients. Unfortunately, a certain percentage of people do not respond to pharmacological therapy. There is no way to predict who will or will not respond to this form of therapy.

Medications

Corticosteroids (Prednisone)

Prednisone is used for suppressing the immune system and inflammation. It mimics the action of cortisol which is produced in the body by the adrenal glands. Prolonged therapy causes the

adrenal glands to stop producing its own cortisol. For this reason when prednisone is discontinued, it must be lowered or tapered gradually to allow time for the adrenal glands to recover. Because Prednisone suppresses the immune system, it can potentially increase the frequency and severity of infections.

The side effects of Prednisone range from annoying to more serious ones. These usually occur with higher doses and prolonged treatment. Most people will experience some of these side affects: they include water retention, and weight gain, puffiness of the face ("moon face"), decreased tolerance to glucose, high blood pressure, muscle weakness, anxiety, depression and sleep disturbance. Cataracts and osteoporosis can occur after prolonged use.

Cyclophosphamide (Cytoxan)

Cytoxan is frequently given in conjunction with Prednisone or may be given alone. While it is usually taken daily by mouth, in some instances it may also be administered intravenously, usually monthly for six months. Cytoxan is an anticancer drug and is used for its immune suppression properties. Because it can lower your white blood count, your physician should monitor your blood count closely during treatment. Cytoxan can also cause bladder irritation due to inflammation (cystitis). Other side effects include hair loss and nausea.

Azathioprine (Imuran)

Although there have been some successful reports in a small number of people, its effectiveness has not been confirmed.

Other Drugs

In the past, Penicillamine, Chorambucil, and Cholchicine have also been used in a small number of patients with uncertain results.

Oxygen Therapy

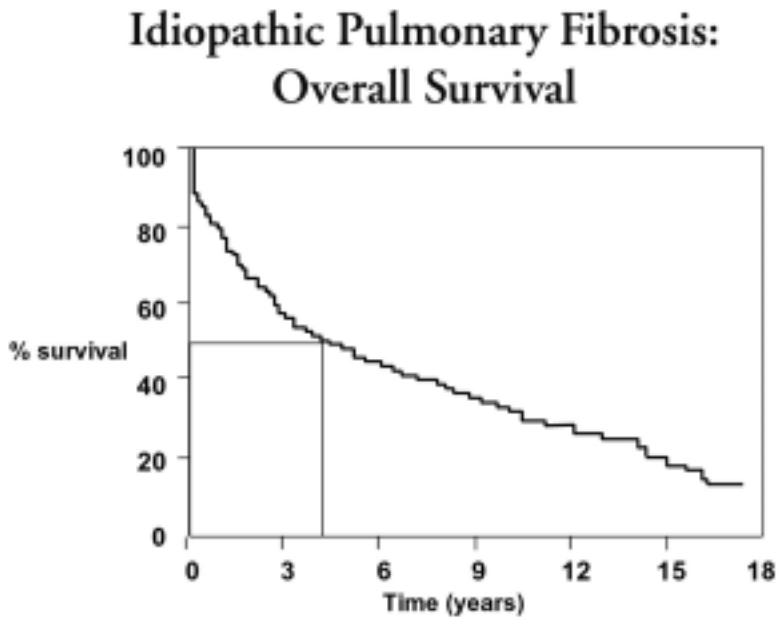
Many patients may require supplemental oxygen particularly when blood oxygen levels become low. This helps to reduce breathlessness, enabling the patient to be more active. Some may need oxygen therapy all the time while others may only need it during sleep and exercise. By testing the level of oxygen in your blood, your physician can tell if you require supplemental oxygen.

Pulmonary Rehabilitation

Pulmonary rehabilitation has become the standard of care for people with chronic lung disease. The aim in pulmonary rehab is to restore the ability to function without extreme breathlessness. These programs offer a variety of services and can be inpatient, outpatient or home/community based. The programs are "multidisciplinary," meaning that the team includes nurses, respiratory therapists, physical therapists, social workers, dieticians, etc. The range of services includes: exercise training; breathing exercises and retraining; anxiety, stress and depression management; and nutritional counseling, to name a few. You need a prescription from your doctor to enroll.

Lung Transplantation

Transplantation can improve both longevity and the quality of life in properly selected patients, particularly for those without complicating medical illness. Because the course of PF is unpredictable and available healthy lungs are limited, early referral is crucial. The waiting period for donated lungs varies and is dependent upon the severity of the disease Transplantation is not without risk and the patient should discuss all the possible complications with their physician. Age restrictions have been removed at some centers.



M Turner-Warwick, Thorax. 1980;35:171

Chapter Eight

What is the prognosis of IPF?

IPF in general has a poor prognosis. The average survival rate is roughly 3- 6 years following onset of symptoms (see graph at left). Survival rates are higher when the disease is diagnosed at an earlier stage, at a younger age and in those who have had a beneficial response to medications. Rapid progression of the disease is associated with cigarette smoking and upper respiratory diseases such as influenza or pneumonia.

The term "average survival rate" is a mathematical one and not medical. There are many individuals who live much longer than six years and others who expire within months after diagnosis. There is a significant correlation between early diagnosis and longevity. It is therefore important to be examined by a competent pulmonologist as soon as the first symptoms appear.

In addition, there are many new developments in both understanding the causes of the disease and the development of effective treatments. Hopefully, these will lead to increased survival time and a better quality of life for those afflicted with Pulmonary Fibrosis.

The most important fact about prognosis is that individuals are unique and people respond differently to treatment. This makes predictions about longevity for any particular person a guessing game. Developing and maintaining a positive attitude will increase survival time for everyone. In addition, enrolling in a pulmonary rehabilitation program teaches you more effective breathing techniques and improves your general physical condition. Being physically and emotionally healthier will increase your longevity. If you are overweight, depressed and are not physically active, you will decrease your longevity.

Chapter Nine

What you can do?

Stay in shape.

The most damaging consequence of lung disease and its sensation of "breathlessness" is the development of an inactive life style. For many patients, activities of daily living like bathing and dressing can create overwhelming fatigue. Air hunger can create panic attacks, and produce negative psychological effects.

People with chronic respiratory problems sometimes limit their physical activities in an attempt to avoid shortness of breath. In addition, family and friends often warn the patient to "take it easy" thinking that doing otherwise is harmful.

The lack of exercise works against you. Inactivity weakens your muscles and they become less efficient. Deconditioning can make even the simplest daily activities more difficult. Through regular exercise muscles become stronger and more resistant to fatigue. With practice and training you can learn to perform tasks in a more efficient manner. By being more efficient you need less oxygen for the same amount of work. The result is that you may find that you have more energy to accomplish daily tasks and that you experience less shortness of breath. A formal rehabilitation program (Pulmonary Rehab) is recommended since there is medical observation during exercise. It also permits the establishment of individualized programs.

Many people breathe ineffectively which causes them to work even harder just to take a breath. During Pulmonary Rehab, breathing techniques are taught which help to improve breathing efficiency and decrease the work of breathing.

Stop Tobacco Use.

Avoiding irritants is a good way to prevent further damage to your lungs. If you are still smoking, the most important thing you can do is to stop. Due to the addictive nature of tobacco, this is can be difficult. Seek the help of your physician to find a smoking cessation class or other beneficial methods to help you.

Second hand smoke can be as harmful as if you were smoking yourself. Family and friends should not smoke around you.

Learn and Practice Relaxation Techniques.

Learning relaxation techniques can help to manage the panic that often accompanies shortness of breath. Joining a support group and/or seeing a counselor can help you cope with your feelings. When you are physically and emotionally relaxed, you avoid excessive oxygen consumption caused by tension.

Anxiety and depression are common in people with chronic breathing disorders. These feelings may aggravate the underlying disease. Many fear losing the ability to function independently and becoming dependent on others. The restrictions on activity due to shortness of breath may lead to isolating oneself from family and friends, adding to the depression.

" *I am still determined to be cheerful and happy, in whatever situation I may be; for I have also learned from experience that the greater part of our happiness or misery depends upon our dispositions, and not upon our circumstances.*"
-Martha Washington

Join a Support Group.

Support Groups are a place where education and information are shared. They are also social events where people can be with others who are undergoing similar experiences. Knowing that you are not alone can provide emotional support. This reassurance can change the way you cope with and feel about your illness. Just knowing that there is someone "out there" who knows just how you feel is comforting. Share ideas, share fears and share joys. When you give out, you always get back.

Participate in your health care.

Remember you are part of a health care team that includes doctors and nurses. They will be asking you a lot of questions. As a member of that team you have a responsibility to do your part. Be prepared to ask your own questions. Be a participant.

Use of Supplemental Oxygen.

All the body's functions depend upon delivery of a steady supply of oxygen. Pulmonary Fibrosis inhibits the transfer of oxygen into the blood stream. Blood oxygen levels are assessed either by Oximetry, which is a device that can be placed over the finger to measure oxygen saturation, or by obtaining blood from an artery, usually in the wrist, to measure blood gases. Perhaps your doctor has prescribed supplemental oxygen based on one or both of these tests. A lot of people are fearful that they will become "addicted" to oxygen. This just is not true.

The body requires a steady supply of oxygen and if it is not getting enough, blood vessels may constrict or narrow. The right ventricle of the heart pumps blood returning from the body into the arteries of the lungs. It must work overtime to pump blood

through these narrow vessels. This results in an increased strain on the heart which can lead to enlargement of the heart with fluid build up in the liver and legs. This is called Pulmonary Hypertension. The symptoms are shortness of breath and dizziness.
It's hard to tell the difference if you are already short of breath. Supplemental oxygen can reduce this strain, help you feel less breathless, improve your sleep and reduce fatigue. If your doctor has prescribed oxygen, use it.

Attitude

Actively participating in all parts of the management of your disease is greatly enhanced by a positive attitude. You may not be able to control the course of your illness, but you do have a some degree of control of your attitude.

Do you want to be positive or negative? Choose one. A positive attitude may not solve all your problems, but it will certainly make a difference in how you cope with having Pulmonary Fibrosis. In addition, studies have shown that a positive attitude will increase your longevity.

> *"A strong positive mental attitude will create more miracles than any wonder drug."* - Patricia Neal

Chapter Ten

Going to the doctor

Arriving at an accurate diagnosis and the best treatment plan requires time. It's like putting the pieces of a puzzle together. It may require several visits and different tests. You can help your physician know about you. Who's lived in that body all these years? Who knows you better than you?

There will be a lot of health care providers on your team in addition to doctors and nurses. Although you have a health care team, you are an important part of that team. As a team member you have certain responsibilities. You will be asked a lot of questions. As a patient, it is sometimes difficult to remember who you talked to and what you said. The first visit to a new physician may produce a lot of anxiety. It's easy to forget something important if you are a little nervous. Try to relax and remember that your teams' purpose is to provide you with the best care possible.

Organize your medical history prior to your visit

Put it in writing, keep a copy for yourself and update as necessary.

1. Frequently the question you are asked are: Why are you here today? What is the reason for this visit?
    a. Start with your symptoms. What are they? Be specific. For example:
        "I have a cough."
        "I'm short of breath."
    b. How long have you had the symptoms?
    c. What aggravates them?
    d. Does anything relieve them?

2. List all medication:
    a. Include prescription and over the counter medications such as vitamins, minerals and herbs.
    b. Include the reason and the how often you take them. Many medicines have multiple purposes. Don't assume "he/she knows" the reason you take each medicine.
    c. Don't rely on others to remember this information for you. What if the other person is not available, in an accident or in the hospital? Then what?
    d. It is sometimes helpful to take all medication(s) with you to show your physician so if there are any questions regarding dosage there will be no confusion.

3. Take a small notebook with you to all visits:
    a. When you ask a question write down the answer. That way, when you get home you won't be frustrated trying to remember what the doctor said to you.
    b. Before each visit, write down questions you want to ask.
    c. Ask about your test results and write down the answer. Never assume that everything is "O.K." if you do not hear from the doctor's office

4. Don't stop prescribed medications on your own, even if your symptoms have stopped.

A sample 3- page medical history form is available for use in the appendix of this document. This does not replace the history taken by your health care team, but is a useful tool. It provides a guide for questions and answers by your team. It helps you to remember important dates, events and symptoms. It's good to keep a copy with you and update as necessary. It is also a good idea to give a copy to a family member as well. If you are ill or have an emergency, your family members will be able to provide correct information regarding your history and medications.

1. List your past and current medical conditions. List medical problems such as diabetes, high blood pressure, heart attacks and cancer. Include information about how long you've had these problems.

2. List all surgeries. Be sure to include dates. List everything. Don't assume it's not important because "it has nothing to do with my lungs."

Chapter Eleven

Research/New Treatments/Antifibrotic IPF Therapies

We apologize for the technical language in which this chapter is written. It was necessary to do so to maintain the scientific accuracy of the information that is included. Please bring this chapter to your physician and allow him/her to discuss with you the concepts and material contained here.

N-Acetylcysteine is a chemical, commonly called NAC, produced by the body that enhances the production of the enzyme glutathione, a powerful antioxidant. NAC helps boost the immune system. NAC is used as a mucus dissolving agent to help break up the thick mucus often present in people suffering from chronic respiratory ailments. In Europe, a large scale clinical trial of NAC therapy with 150 IPF patients is currently underway.

Pirfenidone is an orally active small molecule drug that appears to inhibit collagen synthesis, down regulate production of multiple cytokines and block fibroblast proliferation and stimulation in response to cytokines. Cytokines are small secreted proteins which mediate and regulate immunity and inflammation. They must be produced de novo in response to an immune stimulus. They act by binding to specific membrane receptors, which then signal the cell via second messengers, often tyrosine kinases, to alter its behavior (gene expression). Responses to cytokines include increasing or decreasing expression of membrane proteins (including cytokine receptors), proliferation, and secretion of effector molecules.

Anti Transforming Growth Factor (TGF-B) therapies. TGF-b likely plays a crucial role in the progression of fibrotic disease. It is secreted by activated epithelial cells, macrophages, and endothelial cells in an inactive form bound to latency-associated peptide.

TGF-b is released from latency-associated peptide after it is bound by thrombospondin-1 found in platelet granules or the aVb6 integrin expressed on epithelial cells. The active molecule stimulates fibroblast chemotaxis, differentiation, and collagen synthesis. Pulmonary levels of TGF-b are elevated after intratracheal instillation of Bleomycin in mice and rats. Fibrosis in this model is significantly attenuated by administration of antibodies or soluble TGF-b receptor. TGF-b messenger RNA (mRNA) and protein production is greatly increased in epithelial cells and macrophages of patients with IPF, as are circulating levels of TGF-b. While no therapy currently available specifically targets TGF-b, *Interferon gamma* (IFNg) treatment may lower TGF-b expression in the lungs of IPF patients with an associated improvement in pulmonary function.

Prostaglandin E2. Abbreviated PGE-2, A chemical released by blood vessel walls in response to infection or inflammation. The enzyme mPGES-1 is involved in the production of PGE-2. Other adverse prognostic factors include male gender, advanced disease, and possibly increased release of PGE-2,. from macrophages (Schwartz et al. 1994)

Leukotriene receptor antagonist. The action of leukotriene can be blocked through either of two specific mechanisms: 1) inhibition of leukotriene production and, 2) antagonism of leukotriene binding to cellular receptors.

Endothelin receptor antagonist. An endothelin-receptor antagonist, Bosentan, significantly lowered blood pressure in patients with essential hypertension, suggesting that endothelin may contribute to elevated blood pressure in such patients. Bosentan has FDA approval for the treatment of Pulmonary Hypertension. However it is a “black label” drug which may cause severe injury to the liver.

Anti Tumor Necrosis Factor (TNF) - alpha Therapies. Another mediator likely to play an important role in IPF is TNF-a. TNF-a levels are increased in BAL fluid from IPF patients, and TNF-a production is increased in alveolar macrophages from patients with IPF. TNFa production is also up-regulated in pulmonary epithelia from IPF patients. It is mitogenic and chemotactic for fibroblasts, but in contrast with TGF-b, suppresses collagen synthesis. In response to transient pulmonary overexpression of TNF-a using an adenoviral vector, mice demonstrate a significant inflammatory and fibrotic response. However, in this model, TGF-b production is stimulated soon after infection with the TNF-expressing adenovirus. Thus, it is unclear whether TNF-a acts independently to stimulate fibrosis or merely through its ability to induce TGF-b production. These data are not definitive but suggest a role for TNF-a in the pathogenesis of IPF. As antagonists of TNF-a activity are already in use in the treatment of several inflammatory disorders (e.g., Crohn's disease, rheumatoid arthritis), consideration should be given to testing what effect blocking TNF-a function would have in IPF.

Lovastatin. Lovastatin is one of a group of drugs called statins, which are normally used to lower cholesterol. It is currently being tested for the treatment of Pulmonary Fibrosis. During these tests it was found to potently inhibited granulation tissue formation in vivo. In addition to its proapoptotic effect on fibroblasts, Lovastatin most likely blocked formation of granulation tissue by targeting the action of multiple cellular functions. Several steps in the growth factor signaling cascade are modulated by Lovastatin, including growth factor receptor activity and signal transduction events. A recent study at the Mayo Clinic showed that there was no benefit to the use of statins or ace inhibitors.

There are many additional drugs that have been used to treat other diseases and are now being tested for use against Pulmonary Fibrosis. These are listed on the following page.

GLEEVEC (IMITINAB MESYLATE) belongs to a class of drugs known as tyrosine kinase inhibitors. It is currently being tested for the treatment of idiopathic pulmonary fibrosis at several centers throughout North America. Gleevec has been shown to inhibit lung scarring in laboratory studies with animals. Gleevec's mechanism of action is thought to involve blocking the activity of two growth factors that are important for scar formation, namely platelet-derived growth factor (PDGF) and transforming growth factor beta (TGF-beta). There are no published clinical data on the effects of Gleevec on lung scarring in humans, however, Gleevec has been safely administered to humans who are suffering with leukemia.

Sildenifil (Viagra) Contact: Dr. David Zisman 310-825-8689
Monocycline Contact: Susan Golleher 310-794-6593
Rapamycin Contact Drs. Panos and McCormack at University of Cincinnati 513-475-7510
Thalidomide Contact: John Hopkins, Baltimore, Maryland 410-550-4764
Enbrel Contact: Wyeth Phamaceuticals 800-322-3129
Warfarin (Coumadin) Recent study conducted in Japan produced positive results.

There are many other ongoing research studies. Various government agencies maintain databases on clinical trials. While ClinicalTrials.gov (www.clinicaltrials.gov) contains the most comprehensive listing of NIH supported clinical trials available, not all trials are in the database. Another source of information is the National Heart, Lung and Blood Institute: www.nhlbi.nih.gov. For additional details, please visit the Pulmonary Fibrosis Foundation's website at: www.pulmonaryfibrosis.org

Chapter Twelve

Additional help

You may want to consider joining the on-line support group at:
http://health.groups.yahoo.com/group/Breathe-Support

Contact the Pulmonary Fibrosis Foundation at (312) 587-9272 regarding starting a support group in your area.

There are a variety of websites that contain information on Pulmonary Fibrosis. Some of the information may be valuable while others are unreliable or misleading. The following sites are full of valuable information about Pulmonary Fibrosis.

The Simmons Center for Interstitial Lung Disease
http://simmonscenterild.upmc.com

University of Iowa Health Book
www.vh.org

The National Jewish Medical and Research Center
www.njc.org

Duke University
This site is devoted to Familial Pulmonary Fibrosis.
www.fpf.duke.edu

National Institutes of Health
www.nih.gov

The National Library of Medicine
www.nlm.nih.gov

Various government agencies maintain databases on clinical trials. The NIH through the National Library of Medicine has developed a web site to provide patients, family members and physicians with current information about clinical research.
www.clinicaltrials.gov

The National Home Oxygen Patients Association was established in the late 1990's to give oxygen users the information necessary to lead productive lives.
www.homeoxygen.org

Traveling with Oxygen
www.breathineasy.com

Lung Transplants
www.unos.org

Appendix – Patient Medical History Form

NAME: _____ AGE: _____
PHYSICIAN: _____ DATE: _____

1. What is the reason for your visit today? What are your symptoms?

_____
_____

2. How long have you had these symptoms?

_____

3. Has the respiratory problem: ☐ improved ☐ worsened ☐ stayed the same
Comments:

_____

4. On a scale of 0-5 (0 is not at all, 5 is intolerable), how badly does your problem bother you? _____

5. Does anything make the problem better or worse?

_____

6. Have you changed your life-style or activities because of your respiratory problem?

☐ Yes ☐No

If yes, explain

_____
_____
_____

7. MEDICAL HISTORY (*check all that apply and indicate how long it has been a problem))*

☐ Diabetes_____ ☐ Kidney Problems_____
☐ Arthritis_____ ☐ Thyroid _____
☐ Headache/Migraines_____ ☐ Difficulty walking_____
☐ Heart problems_____ ☐ Dizziness _____
☐ Weakness in legs_____ ☐ Heart attack_____
☐ Epilepsy/Seizures_____ ☐ Back problems _____
☐ High blood pressure_____ ☐ Reflux_____
☐ Neurologic Problems_____ ☐ Stroke_____
☐ Elevated Cholesterol_____ ☐ Anxiety_____
☐ Bleeding tendencies_____ ☐ Ulcers _____
☐ Depression _____

Other medical conditions or hospitalizations not listed here:

_____
_____
_____

8. SURGICAL HISTORY

type of surgery approximate date

_____
_____
_____
_____
_____

9. List Current Prescription Medicines and Over-The-Counter Medicines:

Name of Medication Dosage Reason for Use

_____
_____
_____

11. ALLERGIES:

_____
_____
_____
_____
_____

12. TOBACCO USE:

☐ Never smoked

☐ Yes Packs per day_____ Number of years_____

☐ Do not now but used to smoke

Packs per day_____ Number of years _____
Date stopped _____

Additional comments:

_____
_____
_____
_____

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