Prevent Emphysema Now!

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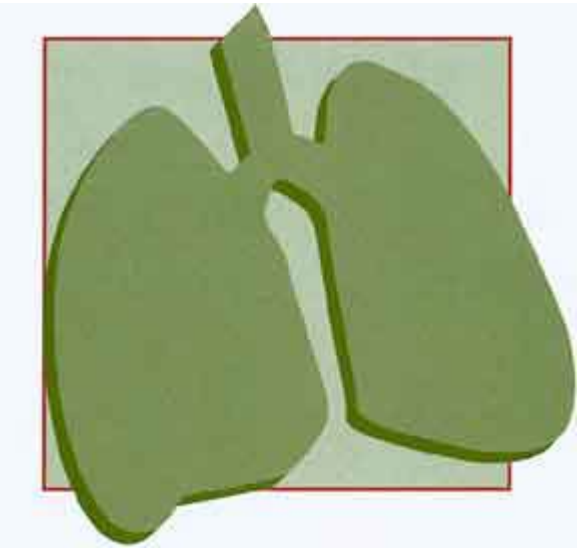

Preface

One of the greatest challenges facing the primary care physician as well as medical specialists today is the growing problem of chronic obstructive pulmonary disease (COPD).

COPD is now the fourth most common cause of death in the United States, and the *only* disease complex in the top ten that continues to rise. Other life threatening diseases, including many cancers, heart attack, and stroke, have benefited by early identification and intervention, with the result that mortality rates are dropping. Thus, the challenge is to identify patients who are beginning to lose lung function early, as an indicator of early stage COPD, which may result in emphysema and death. Prevention of emphysema is the primary goal of the National Lung Health Education Program (NLHEP), and its partner, the American Association for Respiratory Care (AARC). Together, the NLHEP and the ARRC are launching the National Emphysema Prevention Program (NEPP). We invite all primary health care practitioners as well as specialists to join us in our goal to prevent emphysema. Visit our web sites (and_ for the most current information on emphysema.

Undiagnosed COPD

A recent large population-based study, the third National Health and Nutrition Examination Survey (NHANES III), found that a large proportion of patients with COPD have not been diagnosed. This is true despite these patients manifesting symptoms of cough, expectoration, dyspnea on exertion, or wheeze, -- the cardinal signs and symptoms of COPD. Even patients with moderate to advanced stages of disease, may not be diagnosed, and accordingly do not receive treatment. Today, we have a powerful

armamentarium to use in patients found to have early-stage COPD. These therapies can prevent progression into advanced stages of disease. The castrophe of developing emphysema with its life threatening implications, the need for oxygen and possibly surgery, and its tremendous impact on healthcare costs, make early diagnosis and intervention imperative.

Who to Test?

A consensus report of the National Lung Health Education Program (NLHEP), Spirometry Committee recommends simple spirometric testing for all smokers age 45 years, or older. Testing should also be done in anyone with chronic cough, excess mucus, dyspnea upon exertion, or wheeze. These are the major symptoms of COPD which includes a spectrum encompassing asthmatic bronchitis, chronic bronchitis, and emphysema. It is the emphysema component of this spectrum which leads to the greatest impairment and disability. In addition, anyone with a family history of emphysema or chronic bronchitis should have a spirometric test as a part of their data base. Having simple lung function values provide a baseline by which subsequent changes can be evaluated.

We now recognize that spirometry is a simple expression of a complex process. Like blood pressure, spirometry has many determinates, as summarized in Table 1.

Table 1:

Blood Pressure (sphygmomanometry)	Lung Function (Spirometry)
120/80	3.0 FEV_1/4.0 FVC
Cardiac output	Elastic recoil
Cardiac output	Small airways resistance
Blood volume	Large airways resistance
Blood viscosity	Interdependence
Renin-angiotensin axis	Muscular effort and coordination

How to Test?

Briefly, spirometry measures airflow over time. It is most commonly expressed as two numbers which represent volumes expired. The forced vital capacity (FVC), is the amount of air that can be blown out of fully inflated lungs. This is the volume test. The forced expiratory volume in one second (FEV_1), is the amount of air blown out in the first second of the forced vital capacity. The FEV_1, is the flow test. The ratio between the two (FEV_1/FVC), should be more than 70%. If the FEV_1/FVC ratio becomes less than 70%, this is a strong indicator of early airflow obstruction. It is a harbinger of further rapid declines leading to disabling emphysema.

The determinants of expiratory airflow are illustrated in Figure 1. This is an Olm's Law relationship. Expiratory airflow is a function of pressure against resistance. The pressure is generated by elastic recoil and the resistance by the conducting airways. Of course, spirometry is an effort-dependent test. It takes effort to fill the lungs completely, and a complete uninterrupted effort to empty the lungs. Normal lungs empty in about six seconds.

It is now known that the forced expiratory volume in six seconds (FEV_6), is an excellent surrogate for FVC. Thus, doing a six-second expiratory maneuver is more pleasant for the patient and more convenient for the tester. Newer spirometers are now available that use the two parameters: FEV_1 and FEV_6. Predicted values for FEV_6 have been validated and published. These new office spirometers are small and thus portable. They are inexpensive, easy to use, and accurate. Such a spirometer is illustrated in Figure 2.

Figure 1

Factors Associated with Expiratory Airflow

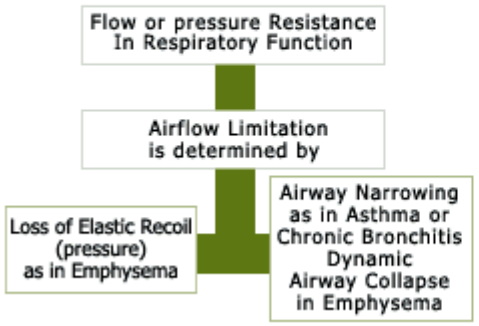

Figure 2

The spirometer illustrated in this photo is inexpensive, accurate and easy to use.

Who to Treat?

Of course, all smokers should stop smoking, but patients who are developing airflow obstruction have an absolutely critical need to *really stop smoking*. Methods of smoking cessation, and other therapies useful in early stages of COPD can change the course of disease.

For example, in the Lung Health Study, patients who stopped smoking, actually had an improvement in FEV_1 with only a slight decline over a five-year follow-up period. By contrast, those patients who continued to smoke had a much more rapid deterioration, (see Figure 3).

However, in the Lung Health Study, no patient died of COPD within the first five years of follow-up. The most common cause of death was lung cancer, followed by heart attack, and stroke, (see Table 2). Thus, finding spirometric abnormalities in heavy smokers is a strong signal to look for other diseases, such as lung cancer, and to institute therapies, such as the control of blood pressure and lipids, to reduce the risk of heart attack and stroke.

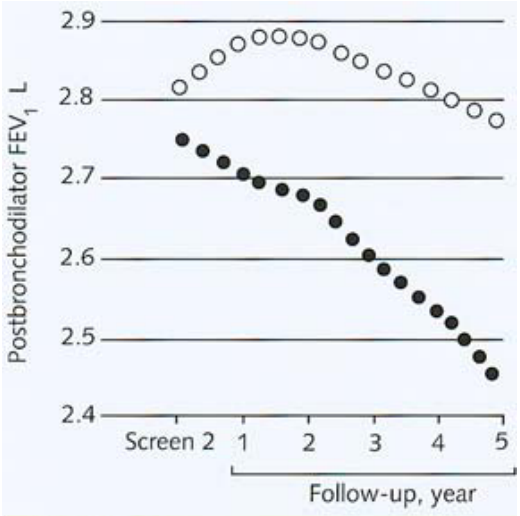

Figure 3

Effect of smoking cessation on FEV_1 over time, as seen in the Lung Health Study. Mean postbronchodilator forced expiratory volume at 1 second (FEV_1), for participants in the smoking intervention and placebo group who are sustained quitters ("), and continued to smoke (!). The two curves diverge sharply after baseline.

Table 2: Causes of Death Within Five Years in the Lung Health Study.

Cause of Death	Smoking Intervention & Ipratropium	Smoking Intervention & Placebo	Usual Care	Total
Lung cancer	**18**	**20**	**19**	**57**
Cardiovascular disease	**18**	**7**	**12**	**37**
Other	**18**	**17**	**20**	**55**
Total	**54**	**44**	**51**	**149**

Adapted from: Anthonisen NR, Connett JE, Kiley JP, Altose MD, Bailey WC, Buist AS, et al: Effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV_1. The Lung Health Study. *JAMA* 1994;272:1501.

How to Treat?

Smoking cessation has been proven to improve lung function and to increase lifespan. It has also been proven to lessen the risk of heart attack, stroke, and after years of quitting, the risk of lung cancer declines. A practical method in smoking cessation is briefly presented below.

The most important stop smoking message is serious counseling about the importance of stopping smoking, and developing a cessation plan. Picking a quit date is key. Nicotine replacement should be started on the quit date. Nicotine replacement products available over-the-counter or by prescription are listed in Table 3.

Table 3: Drugs Used for Smoking Cessation
Food and Drug Administration (FDA), Approved:

Drug and Method of Administration	Unit DoseNicotine pol	Dose Interval
Nicotine polacrilex (oral) * Fifteen to 30 pieces may be chewed over 24 hours.	2-4 mg	Every 1-2 hours*
Transdermal nicotine patch	21, 14, and 7 mg 15, 10, and 5 mg 22 and 11 mg	Over 24 hours Over 16 hours Over 24 hours
Nasal nicotine spray	0.5 mg/inhalation/nostril	8-40 mg/day in hourly or p.r.n. dosing
Nicotine inhaler	10 mg/inhaler	Inhale for 20 minutes 6-16 times/day
Bupropion sustained-release tablets (Zyban®)	150 mg/inhaler	150 mg for 3 days then 300 mg/day
Also Useful:		
Clonidine transdermal patch	0.2 mg	One patch changed weekly for 3 to 10 weeks
Nortriptyline tablets	25, 50, and 75 mg	Maximum dose of 75 to 100 mg per day, treated for 8 to 12 weeks

The non-nicotine product, bupropion, is at least as effective as nicotine replacement in smoking cessation. When nicotine replacement and bupropion are used together, up to a 35.5% biologically proven quit rate can be achieved at one year, compared to a 15.6% success rate with no pharmacologic interventions. When medication is successful, cessation usually occurs within two weeks. Re-treatment is appropriate on those who fail up to seven or eight times.

The retardation of decline in FEV_1 over 50 years has been demonstrated, (see Figure 4). The eleven patients who stopped smoking at age 65 had a survival benefit. Thus, it is never too late to stop smoking, but it is far better to stop at a young age, such as age 45, and before advanced emphysema develops.

Figure 4

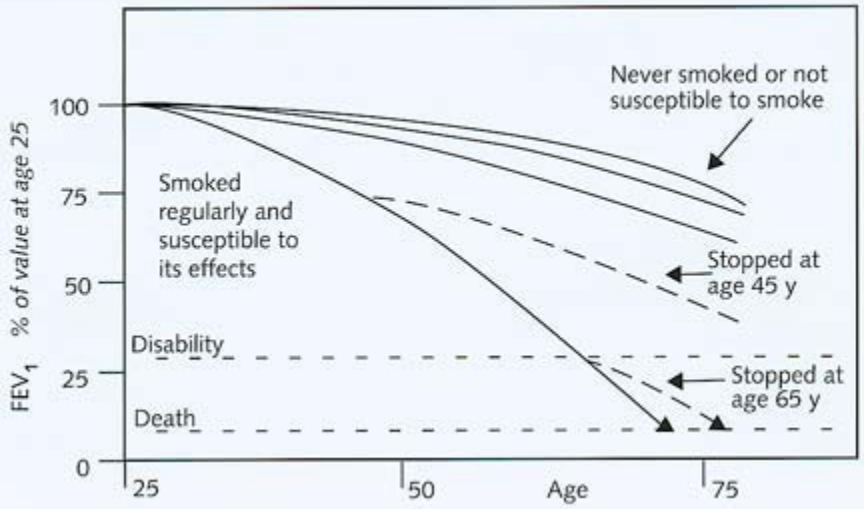

Figure 4: The effect of smoking cessation on decrement in FEV_1 (dotted oblique lines), compared with patients who have never smoked or who are not susceptible to cigarette smoke (upper solid lines), and also compared with patients who stopped smoking late and are deteriorating from the harmful effects of cigarette smoke. The percent FEV_1 when the disability most commonly occurs (approximately 30%), and where death occurs (approximately 10%), are indicated on the dotted horizontal lines. The percent of predicted FEV_1 at age 25 is on the vertical axis and age on the horizontal axis.

From: Peto R, Speizer FE, Cochrane AL, Moore F, Fletcher CM, Tinker CM, et al: The relevance in adults of air-flow obstruction, but not of mucus hypersecretion, to mortality from chronic lung disease. Results from 20 years of prospective observation. *Am Rev Respir Dis* 1983;128:492.

Other Therapy

Influenza virus vaccine should be given every fall to anyone with airflow obstruction. This is particularly important in people over the age of 50. Pneumococcal vaccine should be given at least once in a lifetime, and probably repeated every six years. Today, two new products, oseltamivir (Tamiflu™), and zanamivir (Relenza®), can modify the clinical course of both influenza A and B. Amantadine and Ranitidine are effective only in A strains of influenza.

Inhaled bronchodilators have been shown to work in the majority of patients with early- stage disease. Ipratropium is the first step in therapy. Beta agonists such as albuterol, are also of significant value. Ipratropium and albuterol are available in the same metered-dose inhaler (Combivent®).

A long-acting beta agonistic preparation salmeterol (Serevent®), is compatible with the use of ipratropium. Together, both medications may improve lung function and mitigate symptoms. All patients must learn the proper technique of using metered-dose inhalers or newer inhalation devices coming to the market, for use of anticholinergics, beta agonists, combinations, or corticosteriods.

Inhaled corticosteriods have not been shown to alter the rate of decline in FEV_1 in at least five randomized, controlled, clinical trials. However, inhaled budesonide, fluticasone, and triamcinolone have all been shown to improve symptoms, and to reduce the consumption of healthcare resources in patients with severe COPD. However, a reduction of bone density was found during the conduct of these long-term trials. Thus, any symptomatic benefits should be weighted against potential systemic side effects in the long-term.

Table 4:

Therapy for COPD	
Maintenance Management	
• Stop Smoking	Quit date, nicotine replacement, bupropion
• Inhale Bronchodilators	Anticholinergics Beta Agonists Combination
Exacerbations	
• Antibiotics	Broad spectrum
• Corticosteroids	Systemic prednisone

The empiric use of antibiotics is established in the management of acute exacerbations of purulent bronchitis. Bacterial invasion is often present when following a cold, increased cough, increased sputum volume, and the appearance of sputum purulence (i.e., yellow or green). These common invaders, the aerobics, are H. *influenzae,* S. *pneumonia,* C. *pneumoniae*, and M. *pneumoniae.* These agents are effectively treated with macrolides, fluoroquinolones, second-generation cephalosporins, trimethoprim sulfa, or doxycycline given empirically for five to seven days. A sputum culture is not necessary. Oral corticosteriods, i.e., 40 mg prednisone, or equivalent given for a short period of time, i.e., approximately 14 days, can attenuate the degree of acute airflow obstruction during exacerbations, and can often abort the progression to a severe exacerbation of COPD, thus diminishing the need for hospitalization.

Future Directions

It is now known that the inflammatory mediators involved in the pathogenesis of COPD, leading to airway inflammation and destruction of alveolar walls, are different from those involved in asthma. A number of new pharmacologic entities are being produced to deal with early stage disease. Longer-acting anticholinergic drugs, novel bronchodilators that work through different mechanisms, mucoregulators, and immunomodulators are on the horizon, soon to be released. But, even today, great progress can be made in stemming the worsening of disease in patients with early stages of COPD and related disorders through early identification and intervention. This is why the early identification of airflow obstruction by the routine use of simple office spirometry is of paramount importance. It is in this arena that the primary healthcare practitioner will play a leading role.

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Selected Resources

WEBSITES

American Association for Respiratoty Care (AARC)
Aarc.org

National emphysema Prevention Program (NEPP)
Nepp.org

National Lung Health Education Program (NLHEP)
nlhep.org

MEDICAL ARTICLES

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MEDICAL BOOKS

Simple Spirometry for Frontline Practitioners
Snowdrift Pulmonary Conference, Inc.
1850 High Street
Denver, CO 80218
(303) 839-6755

Frontline Treatment of COPD, 2nd ed.
Book, CD, or audio
Snowdrift Pulmonary Conference, Inc.
Or free from
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877-0368
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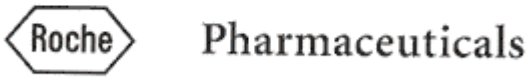

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