COPD*

The Scope of the Problem in Europe

Romain Pauwels, MD, FCCP

In 1995, the European Respiratory Society published a European Consensus Statement on the optimal assessment and management of COPD. In the document, several important areas for future research are identified that may help to increase knowledge of the current situation of COPD within Europe; these include pathophysiology, epidemiology, and the clinical benefits of treatment. This article reviews a selection of important data that have become available since the consensus statement was published, with a specific focus on epidemiology and treatment.

(CHEST 2000; 117:332S–335S)

Key words: COPD; epidemiology; prevalence; treatment

Abbreviations: CCHS = Copenhagen City Heart Study; EUROSCOP = European Respiratory Society study on chronic obstructive disease; ISOLDE = Inhaled Steroids in Chronic Obstructive Lung Disease in Europe; VC = vital capacity

Since publication of the European Respiratory Society consensus statement,1 a number of educational programs have been initiated to raise awareness of COPD and to promote more widespread use of lung function tests in symptomatic patients. COPD, however, remains substantially underdiagnosed, despite epidemiologic studies showing a high prevalence of respiratory symptoms within the general population.

The IBERPOC Project (Estudio Epidemiológico de la EPOC en España) was a population-based epidemiologic study to determine the prevalence of COPD in the general population of Spain.2 This study included 4,035 individuals aged 40 to 69 years who were identified randomly using the population census. The overall prevalence of COPD in this population (comprising 26% current smokers and 24% ex-smokers), defined spirometrically using the European Respiratory Society criteria,1 was 9.1% (of whom 78% were men). Approximately half of the cases were observed in patients aged 60 to 69 years, with the other half divided relatively equally between patients aged 50 to 59 years and 40 to 49 years. Only 22% of individuals found to have COPD had COPD diagnosed previously. However, respiratory symptoms in this population were commonly reported. For example, cough was reported in 13.5%, expectoration in 10.7%, dyspnea after one flight of stairs in 10.4%, and wheezing in 40.2%. Overall, 48% of the population had respiratory symptoms (55.2% of men and 41% of women), which were most frequent in current smokers and least common in never-smokers.3

A high level of respiratory symptoms was also observed in the European Respiratory Society study on chronic obstructive disease (EUROSCOP) population, which evaluated patients with mild or “preclinical” COPD.4 The primary aim of EUROSCOP was to investigate the hypothesis that treatment with an inhaled corticosteroid would affect the decline of FEV1 in subjects with COPD who continued smoking. Following a prolonged run-in period incorporating a smoking cessation program, patients entered a 3-year double-blind trial of inhaled corticosteroid (budenoside) vs placebo treatment.

The study recruited cigarette smokers aged 30 to 65 years of age with mild COPD, defined as post-bronchodilator FEV1 of 50 to 100% predicted, an FEV1/vital capacity (VC) ratio < 70%, and an increase in FEV1 in response to an inhaled β2-agonist of < 10%. The vast majority of patients were recruited via mass media campaigns, with only a few centers recruiting participants via hospital and primary-care records. The EUROSCOP population thus provides an opportunity to examine the prevalence of symptoms in patients with mild airflow obstruction, the majority of whom did not have COPD diagnosed previously.

The study was completed by 1,277 patients (mean age of 52 years), of whom 74% were men. The mean FEV1 of these patients was 77% of predicted, mean

*From the Department of Respiratory Diseases, University Hospital, Ghent, Belgium.
Correspondence to: Romain Pauwels, MD, FCCP, Department of Respiratory Diseases, University Hospital, De Pintelaan 185, B9000 Ghent, Belgium; e-mail: email:romain.pauwels@rug.ac.be

332S COPD: Working Towards a Greater Understanding
FEV₁/VC was 62%, and the degree of reversibility was 2.8%. Individuals had an average of 39 pack-years of smoking and were 17 years old when they started smoking; on average, 22 cigarettes a day were being smoked at entry to the study.

Over three fourths (78%) of the study population with preclinical COPD reported cough and phlegm; individual country prevalence values ranged from 62% in Belgium to 87% in Denmark, where recruitment from within the health-care system was highest and, consequently, the proportion of patients with undiagnosed COPD was lowest. Forty-seven percent of the population reported dyspnea (29% in The Netherlands to 78% in Denmark), 56% reported wheezing (36% in Spain to 70% in Denmark), and 40% reported attacks of dyspnea or cough (17% in Sweden to 62% in Denmark).

Overall, >90% of subjects (from 85% in Spain to 98% in Denmark) had at least one respiratory symptom. There were no significant differences between asymptomatic and symptomatic individuals in age, or in the amount and duration of cigarette smoking. However, percent predicted FEV₁ and FEV₁/VC were significantly higher in asymptomatic patients, compared with symptomatic patients.

Since respiratory symptoms can be evident in patients with undiagnosed COPD, primary-care physicians need to be aware that such symptoms may be indicative of COPD, and that lung function tests should be performed to confirm the diagnosis. As patients who smoke may often not associate their symptoms with early disease, detection of COPD may be improved by primary-care physicians taking the opportunity to ask about relevant symptoms (e.g., cough and dyspnea) when consulting patients for other reasons.

**Factors Affecting Lung Function and Its Decline**

Some interesting insights into the factors that may affect lung function and its decline can be derived from some recently published data from the Copenhagen City Heart Study (CCHS).5 The CCHS, initiated in 1976 and completed at the end of 1992, included men and women ≥ 20 years old living in a defined area of Copenhagen, Denmark. Individuals underwent physical examinations, which included spirometric measurement of lung function, and completed a self-administered questionnaire, which included questions on respiratory symptoms and tobacco smoking.

An analysis performed on data from 6,511 men and 7,712 women showed that socioeconomic status, based on income and education, was associated with lung function, independently of smoking.5 Men with a high income (approximately > $1,400/mo) and >11 years of education had FEV₁ levels an average of 363 mL greater than men with a low income (approximately < $600/mo) and <7 years of education; the corresponding difference for women was 220 mL. Similar results were observed for FVC: differences between the highest and lowest socioeconomic status were 342 mL for men and 221 mL for women. Low socioeconomic index was also associated with a greater risk of subsequent admission to hospital, compared with individuals with a high socioeconomic index.

Reasons for the poor lung function and increased risk of hospitalizations in individuals with lower socioeconomic status may include childhood infections, occupational exposure, and poor housing conditions. Further studies are required to explore whether modifying these risk factors can result in improvements in lung function.

An earlier analysis from the CCHS was able to show how chronic mucus hypersecretion, defined as cough and sputum of at least a 3-month duration for >1 year, can affect the natural history of COPD.6 The population in this analysis included 9,435 individuals examined once between 1976 and 1978 and again between 1981 to 1983. Twelve percent of women (645 of 5,354) and 18% of men (728 of 4,081) had chronic mucus secretion on either or both of these examinations. Mean FEV₁ decline for men without chronic hypersecretion ranged from 30.0 mL/yr in nonsmokers to 45.5 mL/yr in heavy smokers (the corresponding result for women was from 25.4 to 42.7 mL/yr). Chronic mucus hypersecretion at either or both of the surveys led to an increase in FEV₁ decline of 20.7 mL/yr in men and 7.6 mL/yr in women. Chronic hypersecretion was also associated with a significant increased risk for hospitalization due to COPD. The relative risk of hospitalization in individuals with persistent hypersecretion was 5.3 in men and 5.1 in women.6

Although mucus hypersecretion may be associated with a more rapid decline in lung function and an increased risk of hospitalization for COPD, to date there is no conclusive evidence to support the use of mucolytics or mucoregulators in patients with COPD. Currently, the European Respiratory Society does not recommend the use of these agents, but it does highlight the need for studies evaluating the effects of these agents on FEV₁, symptoms, and quality of life.1

**Pharmacologic Treatment of COPD**

The pharmacologic agents used to treat COPD vary among the individual countries in Europe, and
information on treatment patterns can be obtained from analyzing prescription data (M. Rudolf, MD; personal communication; June 1999). In the United Kingdom, the use of anticholinergic agents has increased since 1994, making the United Kingdom one of the higher users of this class of agent in Europe. The Netherlands also prescribes anticholinergics relatively widely, while in Italy and France, the proportion of COPD prescriptions for anticholinergics is approximately one fourth of that in the United Kingdom and The Netherlands. In Europe, the use of β2-agonists has remained relatively stable over the past few years; however, while they comprise approximately 40% of all COPD prescriptions in the United Kingdom, they make up only about 10% of those in Austria.

A major difference in drug use across Europe relates to the prescription of cough and cold preparations. While there are virtually no prescriptions for these agents in the United Kingdom, in Germany and France they comprise approximately one third of all COPD prescriptions. The importance of xanthines in the treatment of COPD also varies from country to country; the percentage of total prescriptions relating to this class of agent in the United Kingdom and The Netherlands is approximately half that of Italy and Austria.

Inhaled Corticosteroids

Despite a lack of conclusive evidence to support the role of inhaled corticosteroids in the management of COPD, the use of these agents is relatively widespread across Europe. The proportion of inhaled corticosteroid prescriptions as a percentage of total prescriptions is highest in The Netherlands, the United Kingdom, and Belgium, but it has grown in Italy, France, Germany, and Austria since 1995.

In asthma, where the inflammatory processes are well understood, inhaled corticosteroids have shown significant benefit. Awareness of the importance of the inflammatory component in COPD has increased in recent years, and it has been hoped that studies of anti-inflammatory agents will show improvements in patients with COPD (especially in lung function, symptoms, and quality of life). Since 1995, three large placebo-controlled trials investigating the use of these agents in patients with severe, mild, and very mild COPD have been completed.7

The Inhaled Steroids in Chronic Obstructive Lung Disease in Europe (ISOLDE) study was performed in the United Kingdom and recruited 751 patients with severe COPD (mean FEV1 of 1.41 L, 50% predicted).8 The patients, 360 of whom were smokers, were randomized to receive placebo or fluticasone dipropionate, 1,000 μg/d, following a short course of oral prednisolone therapy. A total of 401 patients completed the study, which showed FEV1 to decrease over 3 years by 197 mL in the placebo group and by 133 mL in patients receiving inhaled corticosteroids. The reductions in the FEV1 slope were, however, not statistically significant when analyzed in the whole study group.

In the EUROSCOP study, 1,277 subjects with mild COPD (baseline details are presented earlier in this article) were randomized to receive inhaled budesonide, 800 μg/d, or placebo after failing to stop smoking during a cessation program. The decline in FEV1 over the 3-year study period was 180 mL with placebo and 140 mL with budesonide (Fig 1).4 In the corticosteroid group, there was an improvement over the first 6 months compared with placebo. However, the rate of decline from 9 months to the end of the study was similar in the two groups (57 mL/yr with inhaled corticosteroids vs 69 mL/yr in the placebo group; p = 0.39).

The CCHS evaluated the effects of inhaled corticosteroids in a population with very mild COPD.9 Although all patients had an FEV1/VC ratio of < 70%, there was no inclusion criterion relating to FEV1 percent predicted. Consequently, the mean FEV1 value was relatively high (85% predicted), and only 39% of individuals had an FEV1 of < 50% predicted. In this population (76% smokers), inhaled budesonide at a dosage of 1,200 μg/d for the first 6 months, and 800 μg/d for the remainder of the 3-year study, did not improve the rate of FEV1 decline, compared with placebo treatment.

Based on the rate of decline in FEV1, results from these three trials suggest that inhaled corticosteroids are unlikely to be ideal drugs for the management of COPD. However, other factors can also be impor-

![Figure 1. EUROSCOP. The median change from value at randomization in FEV1 with inhaled corticosteroids in mild COPD. Reprinted with permission from Pauwels et al.4](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21947/ on 04/11/2017)
tant to the welfare of patients, including improvements in quality of life and respiratory symptoms, and a decreased frequency in exacerbations. Treatment with fluticasone resulted, in the ISOLDE study, in a significant reduction in the number of exacerbations. Using a disease-specific health-related quality of life measure, ISOLDE showed that inhaled corticosteroids were able to slow the decline of health status.10

**Summary**

Epidemiologic studies examining the incidence of respiratory symptoms indicate that COPD is not only a major health problem across Europe, but it is also underdiagnosed. The potential to increase the rate of diagnosis will arise only through awareness of the importance of symptoms, such as dyspnea and chronic cough or phlegm. Once a diagnosis of COPD has been confirmed, the types of pharmacologic agents used to treat patients can differ substantially from country to country. A consistent observation across many European countries, however, is an increase in the use of inhaled corticosteroids. In contrast to asthma, data reported so far show only modest benefits of inhaled corticosteroids in COPD. Differences between these two respiratory diseases in the response to treatment most likely result from differences in the mechanism of bronchial inflammation. There is thus a need to look for alternative treatment options to improve symptoms, quality of life, and to slow FEV₁ decline in patients with COPD.

**References**

5 Prescott E, Lange P, Vestbo J. Socioeconomic status, lung function and admission to hospital for COPD: results from the Copenhagen City Heart Study. Eur Respir J 1999; 13:1109–1114
10 Spencer S, Anie K, Burge PS, et al. Rate of health status decline is reduced in COPD patients treated with fluticasone compared with placebo [abstract]. Am J Respir Crit Care Med 1999; 159:A524