side stream smoke and the great importance of non-smokers' rights.

These College programs are representative of the unique role that this society has played in smoking cessation in the past 40 years. These efforts include the following: 1) structuring a “health team” approach to smoking cessation with participation of physicians, nurses, and allied health personnel. 2) An ACCP committee prepared national recommendations on the management of smoking in the physicians “workshop.” 3) The College prepared 30 second and 60 second announcements for release on national TV on the critical role of the physician in combating nicotine dependence.

The new look in medicine includes prevention as well as treatment of disease. A top priority of the current and future educational programs and projects of this Society is an emphasis upon combating “the most preventable disease,” the smoking of cigarettes.

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**Oxygen Therapy, Exercise, and Cystic Fibrosis**

**Sh**ort of the situation of acute hypoxemia, the role of oxygen therapy for chronic pulmonary disease remains controversial. In 1980, the Nocturnal Oxygen Therapy Trial (NOTT) Group\(^2\) published results suggesting that, in elderly adults who suffered from hypoxia caused by chronic obstructive pulmonary disease (COPD), continuous oxygen therapy reduced mortality, preserved exercise capacity, and improved neuropsychological function. Many centers treating cystic fibrosis (CF) have tended to extrapolate the recommendations for oxygen therapy in adults with COPD to children and young adults with CF. However, the differences between hypoxemia due to COPD in adults and that due to CF in a younger population are more than just differences in etiology.

In 1989, Zinman and colleagues\(^2\) reported the results of a multicenter study comparing nocturnal oxygen to placebo (compressed air) in children and young adults with advanced CF. During the course of the study, there was a mortality rate in excess of 25 percent in each group, confirming the admission criteria that sought to include only those with advanced disease. Nocturnal oxygen did not appear to decrease mortality, reduce morbidity, or improve exercise ability. However, the group receiving oxygen therapy did continue to remain at work or in school to a greater extent than the placebo group. The authors suspected that this was due to improved quality of sleep for the group receiving oxygen.

While there are a number of criticisms of the NOTT study, not the least of which are the relatively short duration of the study and the low number of hours of oxygen usage per day, the authors did attempt to address the usefulness of supplemental oxygen specifically in patients with CF. The finding that the group receiving oxygen was more likely to continue to lead an active life compared to the placebo group is relatively specific to the age of the patients studied. This was not a factor in the NOTT study, where the mean age of 65 years meant that most patients had retired before entry into the study, albeit early in many cases because of their disease. This serves as another example of differences between young and older patients with advanced pulmonary disease of different etiologies. Clearly the benefits of long-term oxygen therapy may differ depending on the target population, and caution must be used in extrapolating the results of a study in one population to predict results in another.

Another area of growing controversy has to do with the value of exercise in patients with severe lung disease. It has long been appreciated that sedentary elderly adults with advanced COPD can have a dramatic improvement in their day-to-day functioning following a pulmonary rehabilitation program that stresses exercise of graded severity. As exercise performance tends to improve without changes in pulmonary function, the value of mobilizing sedentary subjects has led to a great deal of interest in the concept of “exercise programs.”

Whether the beneficial effects seen in sedentary adults with COPD can be extrapolated into the CF population, who tend to be much more active despite advanced disease, remains to be established. Previous work by Orenstein and colleagues\(^3\) has demonstrated that regular exercise increases physical fitness in patients with CF. Keens et al\(^4\) have shown that upper body exercises, such as canoe paddling, increase respiratory muscle endurance. There are some who believe that regular exercise may substitute for chest physiotherapy in CF. What is lacking is clear-cut evidence that increased physical fitness and/or a regular exercise program results in a reduction in mortality and morbidity. However, for some patients, regular exercise has clearly been associated with an increased sense of well-being and improved body image, and the idea of exercise “prescription” is making its way into the literature.

While clear-cut evidence of the beneficial effects of exercise is still missing, another question concerns
possible harmful effects of exercise in patients with advanced CF. What has been suggested is the potential risk of short periods of desaturation during exercise. Whether this gives rise to worsening cor pulmonale or significant risk of cardiac arrhythmia is unknown, but data that exist, particularly from the point of view of arrhythmia, suggest that this is not a serious risk. Another issue is whether physical activity in advanced CF is limited by hypoxia, hypercapnia, chronic infection, poor nutritional status, poor physical condition, or a combination of all of these factors.

Since marked hypoxemia during exercise has a number of potentially deleterious effects, the degree of desaturation, predictors of severe desaturation, and how it can be prevented have been the subjects of several studies. In 1990, Nixon and colleagues addressed the question of hypoxemia during exercise in patients with CF. They studied 36 patients, who they divided into two groups: those who showed desaturation during exercise, defined as an oxygen saturation (SaO2) or less than 90 percent at peak work on a cycle ergometer (low-saturation group), and those whose SaO2 remained above that level (high-saturation group). The degree of pulmonary impairment of the two groups could be inferred from their mean FEV1, values of 28 ± 8 (SD) percent predicted and 64 ± 16 percent predicted, respectively. Breathing 30 percent O2 during exercise essentially prevented desaturation, which was considerable in room air, as evidenced by values of 92 ± 3 percent at rest and 83 ± 7 percent at peak work in the low-saturation group, but did not improve the ability to do work in either group. During steady-state exercise, the low-saturation group, while breathing oxygen, had a lower heart rate and minute ventilation at the same work load. The end-tidal CO2 tension (PETCO2) was unchanged. For those in the high-saturation group, 30 percent O2 made little difference during exercise, either during the progressive exercise test to peak work or during submaximal exercise. Nixon et al concluded that increases in ambient oxygen minimized exertional desaturation but did not improve exercise performance.

In the present issue of Chest (see page 52), Marcus and co-workers also looked at hypoxemia during exercise in CF. They report the results of supplemental oxygen administration on 22 patients with FEV1 values of 38 percent predicted for the group as a whole (in other words, less mechanical impairment than the low-saturation group reported by Nixon et al but more severe impairment than their high-saturation group). The subjects had been selected on the basis of their having a PaO2 less than 70 mm Hg and a PaCO2 greater than 45 mm Hg or of having had multiple hospitalizations over the previous year. In these subjects, as well as in normal control subjects, peak work was evaluated on a treadmill. As was the case in the study by Nixon et al, the subjects with CF evidenced desaturation when exercising while breathing room air, but administration of 30 percent O2 significantly reduced this degree of desaturation. In contrast to the findings of Nixon et al, Marcus and colleagues found that the CF subjects achieved a higher maximum oxygen consumption and were able to exercise longer when breathing O2 compared to room air. At rest, as a group, the CF subjects had mild hypercapnia and a mean PaCO2 of 46 mm Hg, and their PETCO2 increased during exercise in both room air and while breathing O2 by a mean of 10 and 16 mm Hg, respectively.

The level of hypercapnia in this study is unusual when compared to reported values for PaCO2 and the degree of airway obstruction in CF in the literature. For example, in the study of Zinman et al, the mean FEV1 was 36 percent predicted (in other words, almost identical to the value for the subjects of Marcus et al), and yet the mean PaCO2 was 40 mm Hg. Spier et al reported a mean PaCO2 of 45 mm Hg in a group of patients whose mean FEV1 was 22 percent predicted (in other words, much more obstructed than the patients of Marcus et al). Why hypercapnia was so common in the subjects studied by Marcus et al is unclear, but what is clear from this study and from the studies of others is that breathing 30 percent O2 during exercise very significantly reduces the level of desaturation seen in patients with advanced CF but does not result in clinically significant increases in PETCO2 above the values found during exercise while breathing room air.

What remains to be addressed is whether brief periods of desaturation associated with rigorous physical activity in patients with CF have any short- or long-term harmful effects. Cardiac arrhythmias were not found during these studies, and the concern about worsening cor pulmonale with brief episodes of hypoxia remains conjectural. Should one advise patients with CF who evidence desaturation during exercise to refrain from sports, skiing at high altitudes, or fitness programs? Should oxygen supplementation, often impractical, be mandatory for patients who wish to have such active life-styles? Could we identify specific patients who might be more at risk from brief episodes of hypoxia than others?

In conclusion, the role of oxygen therapy in CF and the therapeutic role of exercise in CF are far from completely understood. There is enough evidence to suggest that extrapolation of data derived in elderly adults with COPD to form a therapeutic approach for younger individuals with CF is fraught with hazard. With the life expectancy of patients with CF increasing, our goal must be to maximize the quality of life despite their advanced pulmonary disease. In such situations, nocturnal oxygen administration (resulting in improved sleep), well-designed physical fitness
programs, and a rational approach to oxygen therapy may play a large part in helping patients to benefit the most from this increased life expectancy. These areas all need more study to give the clinician the proper therapeutic guidelines and risk-benefit relationships.

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The Impact of New Federal Regulations on the Blood Gas Laboratory

The federal government has been very active in the past few years, issuing rules that profoundly affect the ability of blood gas laboratories in the United States to operate. These rules are intended to apply to all clinical laboratories performing blood gas analysis. Coping with these changes is going to be a challenge!

A major problem is sorting through the mountain of documents that have been issued lately.1-7 Most of this has been published in the Federal Register—a total of 227 pages (with very small type). There are two recurring acronyms in these documents: CLIA and HCFA. The first refers to the Clinical Laboratory Improvement Act of 1967 (CLIA '67) and the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88); these are acts of Congress which attempt to ensure quality in laboratory analysis. The Health Care Financing Administration (HCFA) is in the executive branch and is part of the Department of Health and Human Services. The HCFA has been given the responsibility to transform the intentions of Congress into specific regulations.

The intention behind CLIA '67 was to give the federal government oversight of clinical laboratories. However, not all laboratories were covered, and there was no direct federal licensing of laboratories. Nevertheless, these regulations served as standards that inspecting agencies and state surveyors used to rate laboratories.

In 1987 a stir was created in Congress, mostly because of widely publicized reports that PAP smear readings were often unreliable and that shopping mall cholesterol testing was completely unregulated. From these isolated problems, a consensus seemed to develop that all clinical laboratory testing needed to be federally regulated. Both HCFA and Congress acted. The HCFA decided to add more detail (and more teeth) to existing rules based on CLIA '67. A set of proposed rules was published in August 1988, and comments were solicited. A cornerstone of this document was a detailed set of rules regarding proficiency testing. Very specific methods were proposed for providing unknowns to laboratories and for calculating acceptable limits of performance. Proficiency testing programs would have to be federally approved, and only nonprofit organizations would be eligible. Another interesting feature of these proposed rules was that personnel requirements were rather lax; the stated philosophy was that outcome measures, rather than credentials, were to be stressed.

Just a few months later, Congress passed CLIA '88.8 It was short on specifics (this was left to HCFA), but there were key features that set the stage for what has followed:

1. All laboratories that examine human specimens must obtain a certificate (and renew it every two years) to perform a specified set of tests.
2. Proficiency testing programs are mandatory.
3. Laboratories can be sanctioned with license revocation or by means of lesser measures.
4. Certificate fees shall be sufficient to cover operation of the certifying program.

The HCFA decided to finalize its update on the CLIA '67 rules before working on rules pursuant to CLIA '88. In March 1990, the final rule relating to CLIA '67 was published.9 Proficiency testing was required to be in place by January 1991. For blood gas analysis, five vials of proficiency testing materials constitute the quarterly challenge. Eighty percent of the responses for a given analyte (Po2, PCO2, and pH) have to be within "acceptable" limits to be considered "satisfactory" performance. "Unsatisfactory" performance in two of three consecutive quarters is considered "unsuccessful" and subjects a laboratory...