EDITORIALS

Alpha1-Antitrypsin Deficiency

The association of severe α1-antitrypsin deficiency and chronic obstructive pulmonary disease (COPD) was first described by Laurell and Eriksson. This association, which has been confirmed by many authors, was summarized in a recent review. The original work has stimulated extensive investigation of the mechanisms involved in production of experimental emphysema, which has increased our knowledge as to how anatomic emphysema may develop in humans. Additionally, investigation of the possible relationship between an intermediate deficiency of α1-antitrypsin and COPD has been a direct outgrowth of the original description. Since intermediate deficiency is much more common in the general population, the possible association with increased susceptibility to COPD is an important consideration.

At present the clinical importance of intermediate deficiency of α1-antitrypsin remains unsettled. In 1969, Lieberman suggested that subjects who had intermediate deficiency of α1-antitrypsin were at increased risk for the development of COPD. Klayton and associates reported that cigarette smoking seemed to be a determinant for development of COPD in MZ heterozygotes; however, Morse and associates recently presented evidence against the association of intermediate deficiency of α1-antitrypsin with increased susceptibility to COPD, even among cigarette smokers. In their study, the level of α1-antitrypsin was measured by the serum trypsin inhibitory capacity, and phenotypes were not reported.

Intermediate deficiency of α1-antitrypsin may result from the presence of several different genes—P, S, W, Z, null (−), and MDuarte. It is unclear at present whether the absolute level of α1-antitrypsin measured by immunodiffusion or serum trypsin inhibitory capacity is the factor related to development of emphysema. Perhaps the phenotype is an important factor, in that it may reflect differences in the chemical structure of α1-antitrypsin that vary in their ability to inhibit the proteolytic enzymes thought to be responsible for development of emphysema. Possibly, too, the ability to respond to inflammation with an increase in the concentration of α1-antitrypsin may vary, depending on the phenotype present.

This work is of importance to the clinician interested in COPD. A great many people still smoke cigarettes. Something new is needed to motivate them to stop. The Health Belief Model suggests that the patient's belief as to his or her susceptibility to a given disease is important in determining whether an appropriate health-enhancing action, such as cessation of smoking, is undertaken.

If the intermediate deficiency of α1-antitrypsin is shown to increase susceptibility to COPD in smokers, proper explanation to a patient who has such a deficiency might provide the needed motivation to stop smoking. Perhaps a more important and more economical application would be in identified cases of mild COPD. But whether applied to the general population of smokers or to smoking patients with mild COPD, the cost of measuring the level of α1-antitrypsin would be important.

The cost would be related to the test or tests required to identify the susceptible individuals. Is the measurement of the serum trypsin inhibitory capacity or of the concentration of α1-antitrypsin by the radial immunodiffusion method adequate for this purpose? Is the determination of the α1-antitrypsin phenotype alone adequate? Lieberman and associates have reported that measurement of serum trypsin inhibitory capacity or the concentration of α1-antitrypsin by radial immunodiffusion failed to detect 15 percent of the MZ heterozygotes and 60 to 80 percent of the MS heterozygotes. More recently, these workers have also shown that when the MMDuarte phenotype is present, measurement of the phenotype alone fails to detect an intermediate deficiency of α1-antitrypsin. In the present issue (see page 532), they call attention to another situation where phenotyping alone will fail to detect an α1-antitrypsin variant (the M− phenotype) due to the presence of a null gene.

Obviously, additional studies are needed to clarify...
the influence of α1-antitrypsin variants as determinants of COPD in smokers and to determine the tests necessary for detecting these variants. Then the cost effectiveness of more widespread application of measurements of α1-antitrypsin in selected populations can be addressed.

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REFERENCES

Test Your Lungs?

Public awareness that serious chronic disease may be present without symptoms has prompted widespread screening campaigns to identify occult abnormalities. This is particularly true in diabetes, where urine tests are offered, and in hypertension, where individuals are urged to "have their blood pressure checked" at work, at shopping centers, and while seeking medical care for other problems at hospitals, clinics, and physicians' offices. A simple measurement of blood pressure takes only about a minute, is reassuring to the patient when normal, and offers a signal intended to lead to a further, more detailed evaluation if the results are abnormal. Most individuals today know the importance of blood pressure determinations, usually know the accepted normal systolic and diastolic readings, and have begun to recognize that hypertension is an important forerunner of major vascular disease. This has resulted in a healthy awareness of the importance of early identification and remedial therapy among increasing numbers of people.

Like hypertension, the spectrum of chronic pulmonary diseases looms as a major health problem in all industrialized countries. Most pulmonary scientists realize that both chronic obstructive and restrictive pulmonary disease may have a long, relatively asymptomatic or nearly symptom-free interval before sufficient impairment is present to cause the symptoms which result in the patient seeking medical evaluation and care; however, those of us who have spent considerable time studying and treating advanced disease, particularly advanced chronic obstructive pulmonary disease, recognize that although marked benefit can accrue from systematic management, advanced disease is progressive in the long term.

Wouldn't it be better to diagnose disease earlier? Although the answer to this question is clearly not available in terms of studies that establish that the natural history of chronic obstructive pulmonary disease can be altered by management, some hints that functional benefit may be gained already exist in mild and even more advanced degrees of physiologic disorder measured by conventional spirometric tests.1,2

Conventional clinical spirometry is certainly not suited for widespread use. Thus, a need for simple, accurate spirometers suitable for office and clinic use and, in fact, use in the field is clearly present. Waterless electronic spirometers of a variety of designs have recently been developed and marketed. They have been criticized as being inaccurate, but at least one device was found to be quite accurate when tested against a standard Collins water-sealed spirometer.3 Comparison of FVC, FEV1 and MVV (maximum voluntary ventilation) correlated well with simultaneous determinations on the Collins spirometer. The testing procedure might be criticized as a "load" to the flow transducer, but this is a small load and in individual subjects when clinical measurements were made separately on each device at one sitting, no statistically significant differences were present for FVC, FEV1 or MVV. Electronic spirometers must be carefully standardized, of course. A further criticism of electronic spirometers is that they offer a digital readout without a tracing to evaluate the patient's effort or an opportunity to evaluate the full curve. This of course is true, but after all, we accept the blood pressure reading, no