standing bronchitis with marked alterations of clearance there is a decrease of secretory IgA from the high values found in more acute phases of the disease.

R. Fallat commented on sorting patients into types A and B; it depends upon when you look at the patient during the course of his disease. It is a difficult distinction to make in many instances, especially late in the course. The biggest difference in Falk's patients was in severity and frequency of cough. These symptoms are associated with the later phases of both types A and B. Therefore, one has to depend heavily on the accuracy of the history to type those with severe disease.

Pathophysiology of Hereditary Emphysema

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Patients with decreased serum levels of alpha1 antitrypsin were divided into two groups by a quantitative immunodiffusion technique. Patients with levels ranging between 7-15 percent of normal were designated as homozygotes, while patients with levels between 25-60 percent were arbitrarily designated as heterozygotes. Some of these patients were offspring or relatives of homozygotes. Pathophysiologic studies were done to delineate the type of lung disease present and document its presence among heterozygotes.

All homozygotes had severe emphysema characterized by expiratory flow obstruction, hyperinflation and air trapping. Airway resistance was elevated in all but the one nonsmoking patient. Hypoxemia was always present, as well as intermittent CO2 retention. Lung compliance showed marked frequency dependence and lung recoil was always severely decreased (<10cmH2O). Radio-xenon photoscans clearly showed decreased ventilation and perfusion of the lower lobes, while quantitation of these scans confirmed the abnormally high ventilation and perfusion per unit volume of the upper lobes. Delayed washout of the lower lobes was invariably noted.

Homozygotes ranged between 19 and 70 years of age. Clinical or radiologic evidence of pulmonary disease was found only in patients older than 40. However, all patients had pulmonary hyperinflation and decreased lung recoil with frequency dependent dynamic compliance. Forced expiratory flow and lung recoil correlated inversely with age. Radio-xenon photoscans were abnormal only in older patients and the abnormalities were identical to those found in all homozygotes.

Pathologic examination of inflated fixed lungs of three homozygotes showed panacinar emphysema involving 90 percent of the lungs with more severe destruction in the lower lobes. The lungs of one heterozygote who died of unrelated causes showed panacinar emphysema of only 50 percent of the lung with virtually normal upper lobes, except a few scattered foci of centrilobular emphysema.

We suggest that homozygotes develop severe emphysema which involves the lower lobes preferentially and is, therefore, distinct from other forms of emphysema. Heterozygotes can develop identical disease, but at a much older age. Hyperinflation and loss of lung recoil may be the earliest detectable evidence for emphysema in these patients.

Discussion

Macklem commented that he was delighted to see measurement of elastic recoil in Stevens' patients, since it is the most specific diagnostic test for emphysema. The only other disease which may cause this abnormality is a rare case of asthma.

Stevens' method for measuring alpha1-antitrypsin deficiency involved the use of commercially available "partigen" plates and Bering standards. His normal population was derived from hospital employees. Patients were drawn at random from 8000 hospital admissions. They did cellulose acetate screening and then performed the quantitative analysis. These were all patients, not just those admitted for clinical chest disease.

L. Greene commented that there is great variability in the specific activity of commercial trypsin preparations—most being 45-65 percent active trypsin by weight. On this basis it is inappropriate to report the trypsin inhibiting capacity of plasma in terms of "weight of trypsin inhibited." Trypsin preparations should be standardized by an active site titration method to permit comparison of results obtained in different laboratories using different trypsin preparations (Lebowitz J, Laskowski M Jr: Biochem 1:1044, 1962; Chase T Jr, Shaw E: BBRC 29:506, 1967).

Macklem stated that deflation curves correlate well with age; the shape of the curve is important. At higher pressure values normal lung becomes stiffer. It is best to plot them against percent predicted lung capacity.

In answer to a question, Stevens said he would characterize his asymptomatic heterozygotes as type A and the symptomatic as type B.

Asked whether predominance of airway disease in the young is a reflection of proteolytic enzyme release around the airway in the presence of infection, Fallat stated he thought this may be so, but felt that the disease may begin in the blood vessels because defects on lung perfusion scans were among the earliest findings.

W. Thurlbeck asked whether any heterozygotes or homozygotes who become bronchitics have never smoked. The answer from all the panel was that there generally are none. The panel also reported that the oldest homozygotes still in good health were about 45. They all also seemed to feel that smoking is probably the trigger to the onset of clinical disease in heterozygotes, while homozygotes may become symptomatic without smoking.