Epidemiology of Environmentally-Induced Chronic Respiratory Disease

Frank E. Speizer, M.D.

This overview will attempt to carry out three distinct purposes. First, I will review material which describes the natural history of the development of chronic obstructive respiratory disease. I will then briefly mention a number of risk factors, other than cigarette smoking, that must be considered in trying to understand the etiology of both chronic mucous hypersecretion and the development of obstructive airways disease. Third, I will focus on the measurement of air pollution as a risk factor. Since the bulk of the papers to be presented in this session deal with air pollution, I believe it is important to focus our thinking on the difficulties in making these measurements.

NATURAL HISTORY OF DISEASE

Early investigations of the epidemiology of chronic respiratory disease generally started with the diseased patient and retrospectively tried to construct what was believed to be the pathway for disease development. Once the patient had declared himself, measures of pulmonary function generally indicated an obstructive pattern. If the patient was questioned, he would report a series of recurrent episodes of exacerbations of respiratory illness with increased cough and phlegm. Often he would report the onset of his deterioration as resulting from an episode of pneumonia. Further questioning generally revealed a history of chronic cough and phlegm dating back for many years, most often associated with cigarette smoking.

These observations were repeated in a number of countries and led to two hypotheses (Fig 1). The first of these hypotheses was proposed by British workers, and suggested that if the inciting agents could not be removed, then to prevent the development of obstructive disease one had to treat infection, presumably with antibiotics. The second hypothesis, originally proposed by Dutch workers, suggested an alternative mechanism of injury and implied that the use of antibiotics would have little to do with preventing the development of obstructive disease since it was itself an outcome of the development of obstruction.

The difficulty with these hypotheses is that each was based on the assessment of retrospective data and until prospective studies on the natural history of the development of obstructive disease were carried out, they could not be proved.

One such prospective study, carried out in the 1960's on 1,000 working men in London, provides information which allows for a better understanding of the development of chronic respiratory disease. What has become clear is that although almost all subjects appear to be at risk of development of mucous hypersecretion, only 20-40% actually go on to develop significant and disabling obstructive disease (Fig 2). In addition, there are subjects who develop obstructive disease without any mucous hypersecretion. Those subjects who develop only mucous hypersecretion are at greater risk of developing recurrent illnesses with consequent lost time from work. If the inciting agent is

5 Boecker BB, Muggenburg BA, McClellan RO, Clark- son SP, Mares FJ, Benjamin SA. Removal of 144Ce in fused clay particles from the Beagle dog lung by broncho- pulmonary lavage. Health Phys 1974; 28:955-7
6 Dudley RE, Muggenburg BA, Cuddihy RG, McClellan RO. Absorption of diethyleneetriaminepentaacetic acid (DTPA) from the respiratory tract of Beagle dogs. Am Ind Hyg Assoc J 1980; 41:5-11
7 Felicetti SA, Silbaugh SA, Muggenburg BA, Hahn FF. Effect of time post-exposure on the effectiveness of broncho-pulmonary lavage in removing inhaled 144Ce in fused clay from Beagle dogs. Health Phys 1975; 29:89-96

DISCUSSION

Dr. McCusker: Are the mechanisms of the transport of particles to the periphery?

Dr. Muggenburg: We thought that more clearance might take place centrally than peripherally, but there are too many particles in the periphery. I cannot explain the mechanism.

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**FIGURE 1**

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<thead>
<tr>
<th>British &quot;Hypothesis&quot;</th>
<th>Dutch &quot;Hypothesis&quot;</th>
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<tr>
<td>Cigarette Smoking—Air Pollution*</td>
<td>Cigarette Smoking—Air Pollution*</td>
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<tr>
<td>Mucous Hypersecretion (Cough and Phlegm)</td>
<td>Overreactive Subjects</td>
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<td>Recurrent Infection</td>
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<td>Obstruction</td>
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*Occupational exposure was added to each of these hypotheses subsequent to their original development.
removed, often the mucous hypersecretion will remit. Alternatively, those individuals who are likely to develop obstructive disease suffer a more rapid than normal rate of decline in pulmonary function, eventually become disabled and may die of this disease. If the inciting agent (usually cigarette smoking) is removed, the progressive nature of their course may be slowed, but the previously lost function will not be regained. Thus, the identification of subjects susceptible to the development of obstruction before significant obstruction has developed and the removal of the inciting agent might significantly reduce the amount of disability and death associated with these diseases.

**Identification of Risk Factors**

Several categories of risk have been considered in trying to identify subjects at risk of chronic respiratory disease. These factors relate both to the subject as host and his environment. Time does not permit a full discussion of each. They are listed in Table 1. The important point is that few if any of the studies on chronic respiratory disease have tried to consider more than two or three of these factors simultaneously.

**Air Pollution**

Since the bulk of the papers in this session refer to air pollution, I would like to spend the remaining time discussing one aspect of the measurement of air pollution exposure. Generally air pollution measurements are made at a centrally located, convenient monitoring station. Often this station is on the roof of a one or two story public building and often the site is chosen to monitor a major pollution source. When one attempts to monitor actual exposure of subjects, one is immediately faced with the problem that people are mobile and depending how mobile, vary their exposure considerably throughout a day, week or month. Furthermore, most people spend 80% percent of the time indoors and the penetration and sources of the pollutants generated and measured in their environments may vary considerably from pollutant to pollutant.

For example, sulfur dioxide emission basically results from stationary sources using fossil fuels to generate power. Indoors there are few if any sources and thus there are significant gradients between outdoor levels and indoor levels. Factors such as season of the year (whether windows are open or not) presence of air conditioning or the amount of weather stripping used can play a significant role in determining what the levels of exposure might be indoors.

Nitrogen dioxide, which also results from power generation, is also produced by mobile sources such as automobiles. Background outdoor levels are thus driven by these two sources; but a far more significant source appears to be the gas cooking stove. Whereas NO₂ levels in households with electric stoves approximate local outdoor levels, levels in households with gas stoves may be 4-7 times higher. Instantaneous peak levels in kitchens may approach 0.1-1 ppm depending upon the air exchange rates in the kitchen.

Particulate levels indoors may also be driven by outdoor levels. However, indoor levels are significantly affected by the presence of cigarette smokers. A single cigarette smoker will double the particulate level indoors over outdoor levels and two smokers will triple the level. The particulate levels are further complicated by consideration of size fractions, a detailed discussion of which is beyond the scope of this review.

Needless to say, all these factors may significantly alter actual dose as monitored in both air pollution exposure.
and similarly in occupational exposure studies. Thus, as we consider exposure measurements in the subsequent studies to be presented, we must realize just how crude the "state of the art" is in this field. We must recognize that often what we measure can only be used as crude guidelines for monitoring exposure-related health effects.

References

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Discussion

Dr. Becklake: Does it matter whether natural gas or coal gas is used?

Dr. Speizer: I don't think so. At the temperature that the flame burns, NO is formed and rapidly converts to NO2. The only difference is that coal gas also contains carbon monoxide.

Dr. Davis, Vermont: What about stove-heating and wood-burning fuels as a source of indoor air pollution?

Dr. Speizer: They do generate a large amount of particles, which include sodium and potassium sulfates.

Dr. Samet: Heating systems and gas fired water systems are generally vented through the chimney, so a problem would only arise if the stove or fireplace is poorly vented.

Longterm Exposure to Air Pollution and Decline in VC and FEV1*

Recent Results from a Longitudinal Epidemiologic Study in the Netherlands

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A longitudinal epidemiologic investigation on effects of air pollution on chronic nonspecific lung disease (CNSLD) has been conducted in the Dutch municipalities of Vlagtwedde and Vlaardingen. Vlagtwedde is situated in the east of the province of Groningen; it is a rural area without any industrial air pollution. Vlaardingen is a town of around 80,000 inhabitants situated on the northern side of the Nieuwe Waterweg (a branch of the Rhine river) near its entry into the North Sea. The town is polluted by a concentration of oil refineries on the south and southwest side of the river. The air pollution consists of a type characterized by sulphur dioxide (SO2) and smoke, sometimes combined with a type characterized by the presence of oxidants. Since the beginning of the studies, the SO2 levels and the concentration of black smoke have decreased considerably (Fig 1). For instance, at a measuring site in the center of the town (Town Hall), the mean annual concentration of SO2 in 1964 was 229 μg/m3; in 1978, this value was 34 μg/m3. The maximum 24-hour value in 1964 was 555 μg/m3; in 1978, it was 139 μg/m3. The annual mean for standard smoke in 1964 was 46 μg/m3 and was 11 μg/m3 in 1978. Maximum 24-hour values for smoke were 84 μg/m3 in 1964 and 47 μg/m3 in 1978. The air pollution measurements were carried out according to the OECD recommendations. The volumetric method was used, with a flow of 2 m3 per 24 hours (1.5 L/min). The air was collected in dilute hydrogen peroxide and titrated for calculation of the SO2 value. The black stain on a smoke filter was measured by the reflectometer method for standard smoke values. Although the pollution figures are low at present, we fear that the levels will again increase in the coming years, when more coal will again be used. The epidemiologic investigation was carried out in cohorts of about 1,500-2,000 men and women randomly chosen from the municipality registers, who were 15-50 years

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