asbestos via ingestion in animals, OSHA does not believe that the negative findings from these studies negate or diminish the strong evidence from epidemiological studies. OSHA believes that the study of 17,800 insulation workers conducted by Selikoff et al. (Ex. 84-090) carriers considerable weight with respect to the issue of gastrointestinal cancer and asbestos exposure. This study, which found significant excess mortality from gastrointestinal, laryngeal, kidney, and pharyngeal and buccal cavity cancer, had the highest statistical power of all the epidemiological studies reviewed by OSHA.

D. Epidemiologic Evidence of the Risk of Asbestosis From Exposure at the Existing PEL

The existing standard of 2 fibers/cc was established primarily on the basis of an excess risk of asbestosis among workers exposed to asbestos. Since 1972 when the PEL was promulgated, a number of studies with more precise exposure data suggest that a significant excess risk of asbestosis still exists at 2 fibers/cc. The purpose of this section is to review this evidence in light of the revised standard.

This section is organized into three parts. In part 1, asbestosis is described and the variability associated with its diagnosis is discussed with regard to the interpretation of epidemiologic data. In part 2, the disease burden associated with asbestosis is discussed, along with the problems related to the under-ascertainment of cases. Studies that provide data on asbestosis incidence at low exposure levels are critically reviewed in part 3.

1. Introduction

Asbestosis is characterized by diffuse interstitial fibrosis of the lung. It falls into the class of diseases called pneumoconioses and is caused solely by exposure to asbestos. Asbestosis is a progressive disease and, as such, occurs with varying degrees of severity (Berry et al., Ex. 84-20). The signs and symptoms of asbestosis are no different from those of other forms of interstitial fibrosis and, as a result, the diagnosis is subject to differences in interpretation, resulting in both false negative and false positive conclusions.

In unexposed populations, the diagnosis of asbestosis is rare or nonexistent. A history of asbestos exposure is essential to the diagnosis, which is typically made on the basis of physical examination and x-ray evidence and less often by means of accompanying pulmonary function tests. No single sign or symptom predicts the presence of or progression to asbestosis (Murphy, Ex. 84-314; Berry et al., Ex. 84-20). However, selected combinations of signs and symptoms appear to have high predictive value for the progression to asbestosis. Nonetheless, in some cases, minor fibrosis with considerable respiratory impairment and disability can be present without equivalent X-ray changes. Conversely, extensive radiographic findings may be present with little functional impairment (Exs. 84-2, 84-338).

Symptoms of early disease include a non-productive cough and fatigue. As fibrosis progresses, shortness of breath is apparent, even with minimal exertion. Rales, i.e., crackles heard on inspiration, are often present but are non-specific and thought to be no more prevalent in asbestosis than in other fibrotic diseases (Craighead et al., Ex. 84-033). However, in two studies of workers exposed to asbestos, basilar rales occurred with asbestosis in almost all cases (Murphy, Ex. 84-314; Berry et al., Ex. 84-20). Clubbing of the fingers is seen in the late stages of the disease but does not appear to be as specific as other signs or symptoms (Murphy, Ex. 84-314). Cyanosis of the tongue and mucous membranes may also occur in the later stages of the disease (Ex. 84-27).

The roentgenologic diagnosis of asbestosis is based on the presence of small irregular and round opacities distributed prominently in the lower lung fields, accompanied by evidence of pleural fibrosis, pleural calcification, or thickening. Specific details regarding the radiographic features associated with the progression and diagnosis of asbestosis are noted elsewhere (Craighead et al., Ex. 84-033). The presence of crepitations and X-ray changes does not indicate directly that health is impaired, in contrast to the presence of diminished lung function. Typical pulmonary function changes associated with asbestosis include diminished FVC and FEV_1 (Murphy, Ex. 84-314; Berry et al., Ex. 84-20), and, as shown in one study (Murphy, Ex. 84-314), reduced total lung capacity. Evidence does not support a direct relationship between obstructive airway disease, such as is caused by cigarette smoking; rather than by obstructing airways, asbestosis diminishes lung function by restricting the ability of the lung to expand and contract.

Asbestosis is a disease that is irreversible and that evolves and progresses even in the absence of continued exposure. It is not known whether removing an individual from exposure after the appearance of early signs and symptoms will reduce the risk of progression to more severe stages. The probability that asbestosis will progress in the absence of continued exposure appears to be subject to individual variation, as pointed out by Dr. Selikoff:

> What we don't know . . . is whether people who are removed from exposure have less progression than people who continue exposure. I wish we knew that.
>
> There are very few data on this. . . . You can be exposed, have an abnormal X-ray, and either continue exposure or be removed from exposure, and not progress.
>
> On the other hand, you can be removed from exposure and have progression occur. . . . This is an individual reaction (Tr. 7/2, p. 171).

At present, the only reliable means of preventing the occurrence of asbestosis is to reduce the cumulative exposure incurred by individuals during their working lifetimes to a level below which the risk of disease is very low.

2. Excess Morbidity and Mortality Attributable to Asbestosis

The morbidity and mortality of asbestosis have been studied in workers exposed to asbestos. Excess morbidity is determined from the incidence of disease, which is the rate at which new cases of disease are diagnosed for a given number of person-years of observation. It is important to establish the date at which the disease first occurs to accurately estimate the incidence of asbestosis. The mortality rate for asbestosis is the number of deaths due to asbestosis for a given number of person-years of observation. The cause and date of death are determined from death certificates. When a disease has a high case fatality rate; i.e., when the interval between diagnosis and death is short, then the mortality rate and incidence will be similar.

To estimate the incidence of asbestosis, periodic examinations of workers is essential to both identify cases and accurately determine the date of diagnosis. Cases with asbestosis will be missed if they are lost to followup, i.e., cannot be located for examination. If the rate of asbestosis among those who are lost to followup is higher than among those who are examined, a relatively high loss rate can bias the estimate of risk.

The diagnosis of asbestosis can be difficult. It is important, therefore, in epidemiological studies to use standardized methods of diagnosis such as those established by the ILOC. The diagnostic criteria used by different investigators very considerably, and this can account for some of the differences

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