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Association between pleural plaques and coronary heart disease

Ossi Korhola and his co-workers presented an interesting relationship between the occurrence of calcified pleural plaques and coronary heart disease (1). They discussed infection as one possible etiologic factor associated with both conditions. They also emphasized that asbestos exposure is the most important, if not the only, known etiologic factor for pleural plaques.

An increased mortality due to diseases of the circulatory system [code 400–468 of the International Classification of Diseases, 7th revision (ICD 7)] was found among white male textile workers exposed to chrysotile in the United States [standardized mortality ratio (SMR) 1.25, $P<0.05$] (2). The smoking habits were about the same as in a reference group of men in the United States. Some years later, Enterline and his co-workers reported the mortality experience of 1074 white men who retired from an asbestos company in the United States during 1941–1967 (3). The participants were exposed during production or maintenance and followed until 1980. Increased mortality due to coronary heart disease (ICD 7, 420) was observed (SMR 1.12, $P<0.05$) when the cohort was compared with national death rates in the United States.

A cohort of 3211 men first employed between 1933 and 1974 at a Rockdale asbestos textile factory were followed until 1983 (4). A small but not significant increase in mortality due to circulatory disease was observed when the death rate of the cohort was compared with the death rates for England and Wales (SMR 1.15) and the death rates for Rockdale (SMR 1.18).

A cohort of 952 workers first employed between 1930 and 1965 in a chrysotile asbestos mine in northern Italy was followed until 1975 (5). Increased mortality due to cardiovascular diseases (ICD 7, 400–468) was recorded (SMR 1.48, $P<0.01$) when the cohort was compared with Italian national death rates.

A cohort of some 11 000 men born in 1891–1920 and employed for at least 1 month in the chrysotile mines and mills of Quebec was followed until 1988 (6). Ischemic heart disease was more common among those exposed to 300 million or more particles per cubic foot $\times$ years (SMR 1.24) compared with those exposed to less than 30 million particles per cubic foot (SMR 0.92). One part of this large cohort comprising 4559 men was followed for radiological findings (7). Uncalcified pleural changes were associated with an increased mortality risk regarding diseases of the heart (ICD 7, 400–443) [relative risk (RR) 1.54, $P<0.005$]. Pleural calcifications were also associated with a somewhat increased risk of the same disease (RR 1.34, $P<0.10$).

A total of 1106 workers was selected from the workforce of the asbestos industry in Western Australia (8). These workers were exposed to crocidolite, and pleural thickening was a risk factor for death from other causes [RR 1.5, 95% confidence interval (95% CI) 1.3–1.8]. Ischemic heart disease formed the largest proportion of deaths from other causes.

Ischemic heart disease (IHD) was studied in a cohort of 1725 Swedish male shipyard workers exposed to asbestos (9). Men with pleural plaques had a slightly increased risk of IHD when compared with men without pleural plaques (RR 1.3, 95% CI 0.8–2.0) after stratification for age and smoking habits. However, men with asbestosis or suspected asbestosis had a significantly higher risk (RR 3.1, 95% CI 1.5–6.4) of dying from IHD than did men without asbestosis, after stratification for age and smoking habits.

When the deaths of workers exposed to asbestos are compared with death rates from a national population, such a comparison is most often regarded as an underestimation of the true risk as the general population includes sick and disabled people unable to work. This underestimation is well known as the healthy worker effect (10). However, several studies show a relationship between asbestos exposure and coronary heart disease despite this biased comparison. Some studies also show a relationship between the occurrence of pleural plaques and coronary heart disease, and one investigation shows a relation between asbestosis and coronary heart disease.

Does a possible mechanistic link exist between asbestos exposure and coronary heart disease? Human pulmonary epithelial cells cultured in the presence of asbestos crocidolite produced a dose-dependent increase in the secretion of interleukin-6 (11). Interleukin-6 is known to stimulate hepatocytes to produce and secrete fibrinogen (12). A high plasma level of fibrinogen is an established risk factor for coronary heart disease (13). A general hypothesis has linked the inhalation of particles and fibers to the occurrence of IHD in the following way. Air pollutants retained in the lungs after inhalation will hypothetically create low-grade inflammation in association with an increase in plasma fibrinogen. The high concentration of fibrinogen increases the likelihood

for blood clotting and thereby the risk for myocardial infarction and IHD (14, 15).

Thus it seems as if asbestos exposure by itself could explain an increased risk of IHD. However, I agree with Korhola and his co-workers (1) that an infectious agent may be a contributing cause in a series of events creating an inflammatory response.

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