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Occupational exposure to air pollutants, inflammation and ischemic heart disease

by Sjögren B

Affiliation: Work Environment Toxicology, Institute of Environmental Medicine, Karolinska Institutet, SE–177 77 Stockholm Sweden. bengt.sjogren@imm.ki.se

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In December of 1952, London experienced a dense smog. About 12 000 excess deaths were estimated to have occurred from December 1952 to February 1953 because of the acute and persistent effects of the smog (1). In more recent years, the health effects of air pollutants have been studied intensively. Exposure to airborne particulate matter has been associated with increases in mortality and hospital admissions due to respiratory and cardiovascular diseases. These effects have been found in short-term studies, which relate day-to-day variations in air pollution and health, and in long-term studies, which have followed cohorts of exposed people over time (2).

Short-term effects of air pollutants have been studied among 38 million persons in eight European cities. An increase of 10 $\mu g/m^3$ in PM_{10} (particulate matter with an aerodynamic diameter smaller than 10 μm) was associated with an 0.5% (95% confidence interval of 0.2–0.8%) increase in hospital admissions for cardiac causes (3). A cohort of approximately 500 000 persons was formed in 1982 and followed for 16 years. Each 10 $\mu g/m^3$ elevation in fine particulate matter ($PM_{2.5}$) was associated with a 6% increase in cardiopulmonary deaths (4). In an intervention study, the cardiovascular death rate decreased by 10% in Dublin after the ban of coal sales in 1990, which decreased the average black smoke by 36 $\mu g/m^3$ in the city (5). Thus effects have been observed at very low levels of exposure, and it is unclear whether a threshold concentration exists for particulate matter under which no effects occur (2).

During the last decade, more data have linked inflammation to the occurrence of atherosclerosis and thrombosis (6–9). Specific inflammatory diseases have also been linked to the occurrence of ischemic heart disease (IHD). These diseases include viral and bacterial infections [influenza (10), Chlamydia pneumoniae (11, 12), and periodontal disease (13)] and chronic inflammatory diseases such as systemic lupus erythematosus (14), rheumatoid arthritis (15), psoriasis (16), and chronic bronchitis (17, 18).

Elevated levels of inflammatory markers such as fibrinogen, C-reactive protein (CRP), and blood leukocyte count are established risk factors for coronary heart disease (19). In a review, Kamath & Lip (20) concluded that plasma fibrinogen concentration and plasma viscosity are at least as predictive of coronary events as are cholesterol concentration, diastolic blood pressure, and body mass index. Elevated plasma fibrinogen levels have been observed after experimental short-term particle exposure and long-term exposure in an epidemiologic study.

Thirty-eight volunteers were exposed for 2 hours to either filtered air or particles concentrated from ambient air in Chapel Hill, North Carolina. The particle concentration in the chamber during the exposure ranged from 23 to 311 $\mu g/m^3$. Blood obtained 18 hours after exposure to concentrated ambient air contained significantly more fibrinogen relative to that in samples obtained before the exposure (21). The Third National Health and Nutrition Examination Survey (NHANES III), conducted between 1989 and 1994, covered a stratified sample of the United States population (22). Regression controlled for age, race, gender, body mass index, and current smoking. Exposure to PM_{10} was significantly associated with the blood concentrations of fibrinogen, platelets, and white cells when measurements of air pollution and blood concentrations were performed the same day.

In an editorial (23), Nieto concluded that the multifactorial character of cardiovascular disease, the long latency of atherosclerosis (the underlying disease), and the complexity of the process of plaque instability and thrombosis leading to acute events combine to make the task of studying risk factors

particularly challenging. The idea that the inhalation of urban air pollutants may provoke an inflammatory process in the lungs and cause an increase in blood coagulability and, as a consequence, coronary heart disease was hypothesized by Anthony Seaton and his co-workers in 1995 (24). In 1997, this idea was expanded to comprise also occupational air pollutants (25). Ken Donaldson (26) further developed the possible mechanistic aspects of this hypothesis along the following three major lines: (i) inflammation in the lungs caused by particles causes atheromatous plaque development and destabilization, (ii) the inflammation in the lungs causes alteration in the clotting status or fibrinolytic balance favoring thrombogenesis, and (iii) the inflammation causes stimulation of the autonomic nervous system and culminates in alterations in the heart rhythm that lead to fatal dysrhythmia. Furthermore, the particles themselves could enter the circulation and may directly affect the plaques, the clotting system, or the autonomic nervous system.

Today substantial evidence links inflammation to IHD. Smoking is one established air pollutant associated with an increase of inflammatory markers (27, 28) and IHD (29). However, the evidence linking exposure to occupational air pollutants to IHD via a possible inflammatory response is meager compared with the evidence regarding urban air pollutants. The study by Yvon Cormier & Evelyne Israël-Assayag (30) in this issue of the *Scandinavian Journal of Work, Environment & Health* observed a higher leukocyte count among workers exposed to air pollutants in swine confinement buildings but no difference regarding fibrinogen and CRP. All the soluble adhesion molecules were higher among the exposed workers although only one was significantly higher (L-selectin), but these adhesion molecules are weaker risk indicators (31, 32) than traditional inflammatory markers such as fibrinogen, CRP, and white blood cells. Differences regarding the levels of inflammatory markers in this and other studies of farming workers might be explained by different air pollutants and intensities (the level of exposure was not known in this study) and differences regarding adaptation.

Future studies face the challenge of whether inhalation of all types of air pollutants may elicit an inflammatory response in the human lungs and, as a possible consequence, increase the occurrence of IHD. Inhalation of several occupational air pollutants causes chronic bronchitis and lung function impairment. Chronic bronchitis (17, 18) and decreased forced expiratory volume in 1 second (33) are associated with IHD, and future studies should focus on air pollutants as causative agents in these conditions. Blood group O and long-term occupational exposure to soldering, welding, or plastic fumes were all related to an increased risk for IHD (34), and thus blood group O may also be an interesting factor. Studies of the relationship between occupational air pollutants and inflammatory markers, as well as IHD, will increase our knowledge and may increase our scope of potential preventive activities through the reduction of air pollutants.

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Bengt Sjögren, MD
Work Environment Toxicology
Institute of Environmental Medicine
Karolinska Institutet
SE–177 77 Stockholm Sweden
[bengt.sjogren@imm.ki.se]