The Relationship Between Blood Pressure and Environmental Exposure to Lead and Cadmium in Belgium

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The question whether in the general population environmental exposure to lead and cadmium influences blood pressure after controlling for confounding factors remains debated. The environmental exposure of the Belgian population to both lead and cadmium is high as compared with other countries. The Cadmibel Cooperative Study was therefore designed to elucidate whether environmental exposure to lead and cadmium has any effect on blood pressure and renal function in the population at large.

Before embarking on the large Cadmibel project, a small study was conducted. Blood pressure and the 24-hr urinary excretion of cadmium (CdU) and lead (PbU) were determined in a random 4% sample of the population of a small Belgian town. CdU averaged 0.27 µg/24 hr in 46 youths (mean age 14 ± 3 years, ± SD), increased with age, and was higher in 57 adult men (age 41 ± 14 years), as compared with 59 adult women (age 39 ± 14 years) (1.05 vs. 0.81 µg/24 hr; $p < 0.01$). PbU averaged 5.8 µg/24 hr in youths and similarly increased with age; adult men excreted more lead than women (13.3 vs. 8.3 µg/24 hr; $p < 0.001$). Among men, manual workers excreted more cadmium (1.4 vs. 0.8 µg/24 hr; $p < 0.05$) but a similar amount of lead (7.0 vs. 6.9 µg/24 hr) as compared with office workers. In simple regression analysis, CdU was positively correlated with both systolic ($r = 0.30$; $p < 0.05$) and diastolic ($r = 0.38$; $p < 0.01$) blood pressure in women. After adjusting for other contributing variables, however, a weak but negative relationship became apparent between systolic pressure and CdU in women ($p = 0.033$) and between diastolic pressure and CdU in men ($p = 0.047$). In none of the sex-age groups did PbU contribute to the blood pressure variability.

Exposure of the Belgian Population to Cadmium and Lead

The environmental exposure of the Belgian population to both lead and cadmium is high compared with other countries (1,2). In 1981, a cooperative study conducted under the auspices of the World Health Organization (1) assessed human exposure to lead and cadmium in ten countries, including Belgium. The other countries were China, India, Israel, Japan, Mexico, Peru, Sweden, the United States, and Yugoslavia. For practical reasons, this study was not based on random samples of the populations involved. For sake of comparability, groups of teachers were examined in each of the ten countries and their exposure to lead and cadmium estimated from the concentrations of these metals in blood samples. The median blood lead concentration in the Belgian participants in this international study was 152 µg/L and ranked second highest, only exceeded by the median concentration of 220 µg/L found in Mexico. The lowest lead concentration (60 µg/L) was observed in Japan. The position of Belgium with respect to exposure to lead was not

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altered when gender and smoking habits of the subjects in this international study were taken into account. It should, however, be noted that in Belgium a decreasing trend in blood lead has been observed over the last several years: from 1978 to 1986 the median blood lead concentration in the adult population has decreased by 69 µg/L from 170 µg/L to 101 µg/L.

The exposure of the Belgian population to cadmium is also among the highest in the world. In the same international study (1), Belgium, together with Japan, ranked first with a median blood cadmium concentration of 1.2 µg/L. After excluding smokers from the analyses, men from Belgium and Israel had the highest median blood cadmium concentration (1.1 µg/L), whereas nonsmoking Belgian women (0.9 µg/L) came second only to Japanese females (1.2 µg/L). In contrast to lead, since 1981, no significant trend over time in blood cadmium has been observed in Belgium.

Several smaller studies conducted in Belgium (3–6) have demonstrated that environmental exposure to cadmium may lead to an increased body burden and possibly to some biologic effects, at least at the level of the kidney. Indeed, in elderly women having lived in a polluted area (Liège), both the body burden of cadmium and the urinary excretion of proteins, such as β-2-microglobulin, were increased compared to a group of elderly females residing in a nonpolluted control town (Charleroi). In addition, an autopsy study (5) confirmed that living in the cadmium-polluted area augmented the accumulation of cadmium in the kidney. Accordingly, in a retrospective study (6), mortality from nephritis and nephrosis was found to be twice as high in Liège than in Charleroi.

Results of a Preliminary Study

In a small preliminary study (7), a random sample consisting of 4% of all households was identified in a Belgian town with a population of 9000 inhabitants. A total of 274 subjects, aged 10 years or more, were eligible for the study. The response rate was 68%.

Each household was visited twice by the same team of observers. The first home visit consisted of five consecutive blood pressure readings (phase 5 diastolic pressure) obtained with a standard sphygmomanometer in the sitting position, followed by a pulse rate count and a measurement of body weight. A self-administered questionnaire and wide neck, metal-free polyethylene containers for a 24-hr urine collection were given to the participants, who were carefully instructed to keep these containers closed between voiding in order to prevent airborne metal contamination. The questionnaire inquired about the participants' medical history and their current and past occupation, smoking habits, and drug intake. At the second visit 2 to 5 weeks later, the questionnaire and a recent 24-hr urine sample were collected, and the measurements of blood pressure, pulse rate, and body weight were

repeated. Each subject was thus characterized by the mean of 10 blood pressure readings and by two determinations of pulse rate and body weight.

Before use, the containers for the 24-hr urine collections were thoroughly cleansed by bristle and detergent. Thereafter, they were filled with 200 mL of 65% nitric acid and deionized water up to their total volume of 2L and left for 24-hr. Containers were then rinsed five times consecutively, again using deionized water, and dried in an oven. Finally, 10 mL acetic acid (99–100%) and 200 mg thymol were added to the containers, which were tightly closed before storage. Before use in the study, a random sample of the prepared containers was checked for cadmium and lead contamination and none was found to be positive. When 24-hr urine samples were returned to the laboratory, an aliquot of 50 mL was transferred to a small container and kept frozen at –20°C until analyzed.

The 24-hr urine samples were analyzed for cadmium, lead, sodium, potassium, and creatinine. The cadmium and lead concentration in urine were measured as described previously (8), using a Perkin-Elmer, Model 305 atomic absorption spectrophotometer equipped with a deuterium background correction system and a Perkin-Elmer HGA-74 atomizer unit.

The urinary excretion of cadmium averaged 0.27 µg/24 hr (geometric mean) in 46 youths (mean age ± SD, 14 ± 3 years), increased with age, and was significantly higher in 57 adult men (age 41 ± 14 years), as compared with 59 adult women (age 39 ± 14 years) (1.05 vs. 0.81 µg/24 hr; $p < 0.01$). Urinary lead averaged 5.8 µg/24 hr in youths and similarly increased with age; adult men excreted more lead than women (13.3 vs. 8.3 µg/24 hr; $p < 0.001$). Among men, manual workers excreted more cadmium (1.4 vs. 0.8 µg/24 hr; $p < 0.05$), but a similar amount of lead (7.0 vs. 6.9 µg/24 hr) as compared with office workers. In simple regression analysis of urinary cadmium in women was positively correlated with both systolic ($r = 0.30$; $p < 0.05$) and diastolic ($r = 0.38$; $p < 0.01$) blood pressure. After adjusting for other contributing variables (age, body weight, smoking habits, urinary potassium excretion, urinary β-2-microglobulin concentration), a weak but negative relation became apparent between systolic pressure and urinary cadmium in women ($t = -2.21$; $p = 0.033$) and in men between diastolic pressure and the urinary cadmium excretion ($t = -2.04$; $p = 0.047$). These correlations between blood pressure and the urinary excretion of cadmium do not necessarily imply a causal relationship, since an unknown third factor might be the common link that produces the association. The association could also be explained by the hypothesis that subjects with a higher blood pressure are less able to eliminate cadmium in their urine. Finally, these correlations could indicate that cadmium, even at its usual environmental concentration, might have some sort of biological action and, for yet unknown reasons, lowers blood pressure. By contrast to cadmium, in this preliminary study (7), the urinary

lead excretion did not contribute to the blood pressure variability in any of the age-sex groups involved.

Cadmibel Study

In view of the high exposure of the Belgian population to both cadmium and lead (1–6), four research groups* planned and designed a large cooperative study to elucidate the possible effects of environmental exposure to cadmium and lead on blood pressure and renal function in the population at large. The Cadmibel project is a cross-sectional population study, which principally addresses the following questions: a) Is it possible to demonstrate in the general population an association between the degree of environmental exposure to lead and cadmium and the body burden of these metals? b) Does an increased body burden of lead and cadmium lead to an elevation of blood pressure and/or a higher prevalence of renal dysfunction in the general population? c) If it is possible to demonstrate that environmental exposure to lead and cadmium entails biologic effects, what is the critical internal dose above which the population may be at risk?

Collection of Data

The Cadmibel Study is being conducted in two areas with confirmed environmental pollution by cadmium and in three control areas with low environmental exposure to cadmium. The polluted areas are Liège (industrial and urban) and Noorderkempen (industrial and rural). The control areas are Brussels (urban), Charleroi (industrial and urban), and Hechtel-Eksel (nonindustrial and rural).

In these areas, random samples of the households were identified. Subjects aged 20 years or more were eligible for the study. Sampling was performed in such a way that a similar number of subjects of either sex was recruited in each of the age groups 20 through 39 years, 40 through 59 years, and 60 years or more.

All eligible subjects were visited at their homes by trained observers in order to obtain on each of two separate occasions five blood pressure readings, a pulse rate count, and anthropometric measurements. Self-administered questionnaires were used to collect in-

formation about present and past confounders such as residence, medical history, medication, smoking, alcohol intake, food habits, professional occupation, and possible exposure to several trace elements. The concentration of heavy metals was determined in blood as well as in spot and 24-hr urine collections, applying internal and external quality controls. Finally, renal function was estimated from measurements of creatinine, β-2-microglobulin, retinol binding protein, albumin, and proteins in blood and/or spot urines and in 24-hr urine collections.

From September 1985 to December 1987, about 2000 subjects, representing 80% of those eligible, participated in the study. The project will be continued in a rural and urban nonpolluted control area. The field work will be completed by the end of 1988, and then statistical analyses of the data will begin.

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