

# Contribution of Cigarette Smoking to Cadmium Accumulation in Man

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LEWIS et al. (1972a, 1972b) demonstrated a positive association between amount of cigarettes smoked and the cadmium burden of lungs, liver and kidney combined. Such a relationship was previously predicted by FRIBERG et al. (1971). An independent replication of the study by LEWIS et al. was performed in a separate autopsy population.

## MATERIALS AND METHODS

An autopsy survey of a few trace metals was applied to a population of North Carolina residents. One hundred and six autopsies occurring during the first half of the year 1971 on persons ranging in age from 16 to 91 years were contributed by seven hospitals in central and eastern North Carolina. The hospital population represented by the study sample had an autopsy rate well over 60%. Although little selection was exercised in the acceptance of autopsies into this study, some preference was given to white males having died of cardiovascular disease. After weighing of the lungs, liver and kidneys, a site for tissue sampling was chosen in a pre-determined manner for each organ or organ pair; when this site showed gross pathology, the nearest normal-appearing site was used instead.

Preconcentration. Wet samples of 2-4 g were weighed and freeze-dried for 8-12 h. Tissue samples were cut up and freeze-dried. The freeze-dried samples were weighed and placed in an International Plasma Corporation Model 1101 plasma machine. Ashing conditions were typically 300 W of forward power (50

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W/chamber) with 300 ml/min oxygen flow. Ashing time was 8-12 h at a temperature below 250° C. The ashed samples were removed from the asher, cooled, weighed and transferred to plastic-capped glass vials.

Manipulation of Ash. The sample ash was weighed to give a final analyte solution that was 2 mg of ash per ml solution. Samples with sufficient ash were made up to 5.0 ml. Samples were dissolved with glass-distilled water. A 1:10 dilution of this solution was made for the analysis of the metal cadmium.

Chemical Analysis. The metal cadmium was analyzed by atomic absorption spectroscopy using direct aspiration of the dissolved ash samples. Analysis was made using calibration curves, after analysis by standard addition revealed that, within the precision of the analysis, no matrix interferences were present.

Precision of the Analytical Technique. Precision of the atomic absorption technique was assessed by analyzing replicate solutions. It was a function of the absorption values (concentration) and of the background noise. Typical values (these varied somewhat due to non-constant noise levels) for the relative standard deviation were, for the high and the low range of concentration, 5-25%.

Age, race and sex were obtained from hospital records or death certificates. Usual residence, smoking habits and occupational exposure were obtained via a short questionnaire sent to the relatives of the decedents (FIGURE 1). Completed responses were received for 69 autopsies (64%). Cases with incomplete trace metal data (due to unavailability of some of the organs or to technical difficulties) were removed from the study. Also removed were two cases with death causes known to interfere with trace metal metabolism (a case of acute pancreatitis and a case of scleroderma). Thus 62 cases remained in the study. The autopsy population is described elsewhere (VOORS et al. 1973).

Because present knowledge concerning the cadmium content of cigar and pipe tobacco is incomplete, heavy cigar or pipe smokers (more than 5 per day) were excluded from the study. The remaining 55 cases were classified as to smoking history as follows. Classification was based on relative's response to the questionnaire, and represents the amount of cigarettes smoked daily during the five years preceding death, as

What was the decedent's occupation for most of his adult life? (Check one box)

- ☐ Farming, fishery, forestry and related occupations
 ☐ Bench work, machine trades and processing  
☐ Clerical and sales
 ☐ Construction work  
☐ Professional and managerial
 ☐ Other, specify

Please briefly describe the main kind of work he did in this occupation:

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Was he frequently exposed to irritating smoke, dust, or fumes at his job?

- ☐ Yes
 ☐ No

If yes, please list them.

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For the last five years of his life, how much did he smoke each of the following (check only one box per line):

Type of Tobacco	Yes, Regularly (5 or more per day)	No, Never Smoked	Yes, Occasionally	No, Ex- Smoker
Cigarettes				
Cigars				
Pipe				

If he did smoke cigarettes, did he usually inhale? ☐ Yes ☐ No

If he did smoke cigarettes, about how many a day did he usually smoke when he was smoking?

- ☐ Less than ½ pack per day (1-5 cigarettes)
 ☐ About 1½ packs per day (26-34 cigarettes)  
☐ About ½ pack per day (6-14 cigarettes)
 ☐ About 2 or more packs per day (35 or more cigarettes)  
☐ About 1 pack per day (15-25 cigarettes)

FIGURE 1. Parts of questionnaire used for male decedents.

expressed in packs per day (never smoked, less than half a pack, half a pack, one pack, 1½ pack, two or more packs per day). When light cigar or pipe smoking occurred in combination with cigarette smoking, it was classified according to the number of cigarettes only. When it occurred without cigarette smoking, it was included in the "less than half a pack" category. Ex-smokers (no smoking during the preceding five years) were arbitrarily assigned to the same category.

Organ cadmium concentrations per wet weight were multiplied with the reported organ weight. Thus, for each individual a combined organ burden index was calculated from summed values (kidney + liver + lungs), conforming to the study by LEWIS et al.

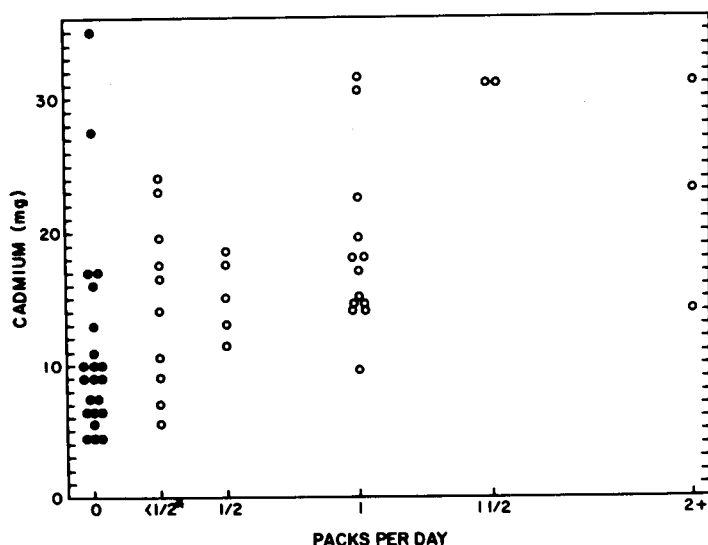


FIGURE 2. Cadmium accumulation (as expressed by combined organ burden) related to the amount of cigarettes smoked during the last five years. Autopsy study population, North Carolina, 1971.

O = Cigarette smokers                      ● = Non-smokers

\* Including ex-smokers and light non-cigarette smokers

After logarithmic transformation of all above data for the purpose of obtaining Gaussian distribution, product-moment correlation coefficients were computed.

## RESULTS

FIGURE 2 shows the relationship between cigarette smoking history and cadmium accumulation as expressed by combined organ values. The geometric mean combined value for non-smokers (9.6 mg, S.E.M. = 1.1 mg) is lower than for smokers (16.2 mg, S.E.M. = 1.1 mg). Assuming arbitrarily that the smokers of two or more packs of cigarettes smoked exactly 2½ packs per day, the coefficient of correlation between combined organ burden and cigarette smoking is 0.56, which is statistically significant at the 0.1% level (TABLE 1).

TABLE 1  
CORRELATION OF VARIOUS CADMIUM BURDEN INDEXES  
WITH CIGARETTE SMOKING,  
AUTOPSY STUDY POPULATION, NORTH CAROLINA, 1971

Cadmium Burden Index	Coefficient of Correlation+ with Cigarette Smoking
Lung burden	0.26*
Liver burden	0.26*
Kidney burden	0.63**
Composite burden index	0.56**

+ Product-moment correlation coefficient computed  
after logarithmic transformation of the data  
(n = 55)

\*  $P \approx 0.05$

\*\*  $P < 0.001$

Considering the cadmium burdens of the various organs individually as to their correlation with cigarette smoking, it was found that lung and liver have a correlation coefficient which is bordering on statistical significance at the 5% level, whereas the correlation coefficient for the kidney is highly significant at the 0.1% level.

In a multiple regression analysis, giving consideration to age of death, race, sex, combined organ burden, and smoking, the age, race and sex were found not to alter the primary association between cadmium burden and smoking. Similarly, when reported exposure to fumes was taken into account, the persons thus exposed showed no significant difference with the non-exposed persons, and this was also true when smokers and non-smokers were analyzed separately (TABLE 2).

TABLE 2

GEOMETRIC+ MEAN CADMIUM ACCUMULATION (in mg),  
BY CIGARETTE SMOKING AND BY EXPOSURE  
TO IRRITATING SMOKE, DUST OR FUMES.  
AUTOPSY STUDY POPULATION, NORTH CAROLINA, 1971

Exposure to Fumes, etc.	Non-smokers	Smokers	All
No	8.7 (15)	15.2 (23)	12.2 (38)
Yes	11.6 (7)	18.8 (10)	15.4 (17)
All	9.6 (22)	16.2 (33)	13.1 (55)

+ None of the vertical group differences is statistically significant at the 5% level. Numbers of persons observed are in parentheses.

#### DISCUSSION

LEWIS et al. (1972a) concluded from their findings that tobacco smoke constitutes a major source for cadmium accumulation in man. This finding is of interest because such an association can be used to elucidate by means of population-based data the questionable pathogenicity of cadmium, and at the same time perhaps to contribute to knowledge concern-

ing the role of tobacco smoke in associated disease processes. Therefore, an independent replication of this finding was undertaken in the present study.

The smoking histories used in this study pertained only to the five years preceding death, and hence do not lead to the more complete data reported by LEWIS et al. Nevertheless, if there is any excretion of cadmium proportional to the body burden, the more recent smoking history may indicate the amount of cadmium retained from smoking (KJELLSTROEM 1971). With this proviso, our findings are in good agreement with the results of LEWIS et al. in demonstrating a clear association between cigarette smoking and combined organ burden of cadmium.

#### SUMMARY

A North Carolina autopsy population was examined for cadmium level in lung, liver and kidney. A questionnaire on the smoking habits and occupational exposure of each decedent was sent to the nearest relative. Analysis of these data indicates a positive association between cigarette smoking and body burden of cadmium as indexed by the organs, thus confirming the work by LEWIS and colleagues, who concluded that tobacco smoke constitutes a major source for cadmium accumulation in man.

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