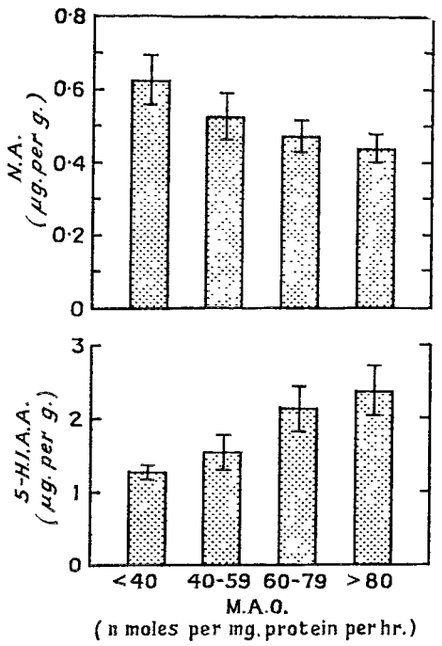

Fig. 3—Relation of hindbrain-M.A.O. activity to mean concentrations (±S.E.M.) of N.A. and 5-H.I.A.A.
There is a signficant negative correlation of N.A. and positive correlation of 5-H.I.A.A. with M.A.O. activity.
N.A.: $n=-0{\cdot}54$, $P<0{\cdot}005$. 5-H.I.A.A.: $n=+0{\cdot}55$, $P<0{\cdot}005$.

three human sources of M.A.O. are consistent in showing a positive correlation of enzyme activity with age in human brain, platelet, and plasma. This, plus the age/M.A.O. correlation in animals, suggests that this age-related increase in M.A.O. is a general biological phenomenon. The fact that N.A. concentrations correlated negatively and 5-H.I.A.A. concentrations correlated positively with brainstem-M.A.O. activity suggests that this enzyme may play a major role in regulating intracellular concentrations of biogenic amines. Therefore the increased levels of 5-H.I.A.A. in the cerebrospinal fluid of elderly patients observed by Bowers and Gerbode [10] may be a consequence of increased levels of brain-M.A.O. Furthermore, we observed a significant linear decrease in hindbrain-N.A. levels with age. The correlation of N.A. levels with age would be consistent with the hypothesis that these age-related decrements of N.A. levels were a consequence of the age-related increase in M.A.O. activity.

Our findings of an association of M.A.O. activity and substrate levels with age make it imperative that age be controlled in studies of clinical material involving brain tissue or cerebrospinal fluid, particularly in the investigation of the biogenic-amine theory of depression and parkinsonism. Numerous epidemiological studies have established that the prevalence of depression increases with age. The fact that M.A.O. levels also increase with age makes it tempting to speculate that this relation of age to enzyme activity might be a predisposing factor to depression which accentuates changes in brain amines precipitated by other events.[19] Similarly, the age-related changes in M.A.O. may play a role in the pathogenesis of parkinsonism.

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References at foot of next column

Preliminary Communication

CONTRIBUTION OF CIGARETTE SMOKING TO CADMIUM ACCUMULATION IN MAN

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Summary Cadmium, a non-essential, potentially toxic metal, accumulates in human tissues with increasing age. Because many foods contain cadmium, the diet has been considered the major source for man. Cigarette tobacco contains appreciable amounts of cadmium, which on burning passes into the smoke. Analysis of necropsy material has shown that non-smokers accumulate smaller amounts of cadmium in their organs than smokers. In addition, the accumulation in smokers is related to the number of pack-years smoked. It is concluded that tobacco constitutes a major source for cadmium accumulation in man; and in heavy smokers, inhalation of the cadmium contained in tobacco smoke may make a greater contribution to the total body burden than the amount derived by dietary intake.

INTRODUCTION

MUCH concern has been expressed in the past few years regarding the inadvertent exposure of the general population to toxic trace metals. Many of these (e.g., lead, mercury, and cadmium), once having gained entry into the body, are retained for a long time. Great efforts have been made to identify their sources so that effective preventive measures can be undertaken.

This report reviews an association found between cigarette smoking and the cadmium content of wet-ashed tissue samples obtained at necropsy.

MATERIALS AND METHODS

In a consecutive series of 172 adult necropsies, data were

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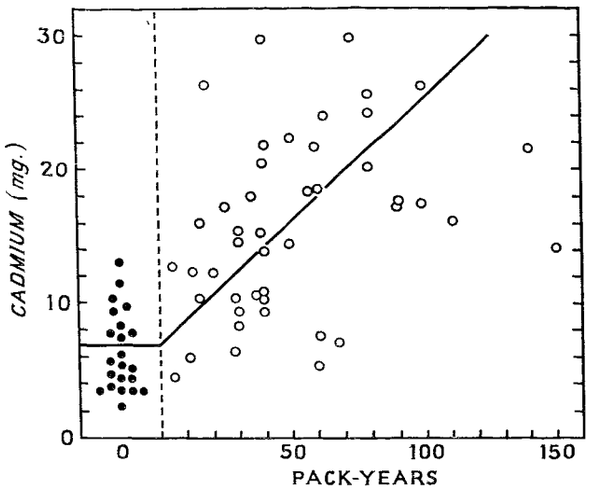

Cadmium accumulation (as expressed by composite values) related to cigarette smoking.
○ =Cigarette smokers. ● =Non-smokers.

collected on smoking habits and occupation (subsequently classified as either blue or white collar), using as the information source either the hospital clinical record or the immediate next of kin. The number of years smoked as well as number of cigarettes smoked per day were known on each of 45 male smokers (mean age at death, 60 years, S.E.M. = 1·6). This allowed calculation of the number of cigarette pack-years smoked by each. The series also included 22 male non-smokers (mean age at death 60 years, S.E.M. = 2·7). The cadmium concentration in kidney, liver, and lung samples (μg. per g. of wet tissue) removed from each subject was measured by atomic absorption spectrophotometry using a Perkin Elmer 303 instrument with a Boling triple-slot burner and an air-acetylene flame. Knowing the weights of each subject's organs, it has been possible to estimate the total cadmium content (mg.) of each organ. The composite of these for each subject (kidneys + liver + lungs) gives an index (about 45–50%) of the total body burden.

RESULTS

The accompanying figure shows the relationship between cigarette-smoking history and cadmium accumulation as expressed by composite values. The mean composite value for non-smokers (6·63 mg.; S.E.M. = 0·64) is lower than that for smokers (15·80 mg.; S.E.M. = 1·04). The diagonal line indicates the level of cadmium content for a given cigarette exposure and is based upon a regression equation ($y = 8{\cdot}54 + 0{\cdot}12x$) with a statistically significant slope ($P < 0{\cdot}001$). In a multiple-regression analysis giving consideration to age at death as well as composite cadmium content of organs and number of pack-years smoked, age was not found to alter the primary association between cadmium accumulation and number of pack-years smoked. Similarly, when occupation was taken into account, although non-smoking blue-collar workers showed a slightly greater mean composite value than non-smoking white-collar workers—i.e., 8·14 mg. (n = 11) *v.* 5·27 mg. (n = 11) ($t = 2{\cdot}37$, $P < 0{\cdot}05$)—comparison of the mean composite values found in cigarette-smoking blue and white collar workers showed no significant difference —i.e., 16·40 mg. ($n = 28$) *v.* 14·86 mg. (n = 17) ($t = 0{\cdot}68$, $P = 0{\cdot}5$).

DISCUSSION

Because fish food (especially crustacea), certain grains (e.g., wheat and oats), and many dairy products contain measurable amounts of cadmium, food has been considered the major source of cadmium for the population at large. It has been estimated that on average, 3 μg. of cadmium is retained in the body per day [1] (based on the observation that the average adult has a total body burden of 30 mg.[2]). Our data would suggest that non-smokers accumulate much less than this (i.e., 1 μg. or less per day), and that the estimate of 3 μg. per day is due to the inclusion in previous studies [3,4] of a mixed population of smokers and non-smokers. It would seem that for each cigarette pack-year, smokers accumulate through inhalation an additional 0·5 mg. of cadmium (i.e., 1·5 μg. per day) above that accounted for by the dietary source alone. Cigarette tobacco contains an appreciable amount of cadmium [1,5,6] (>1 μg. per cigarette), of which 70% passes on burning into the smoke.[5,6] Absorption of a small part of this (10%) would be sufficient to produce an increment in cadmium accumulation to the extent of 0·5 mg. per pack-year.

Our findings could also help to explain the intriguing pattern of cadmium accumulation known to occur in man with increasing age.[1] A newborn baby has virtually no cadmium in his tissues,[7] but with maturation the element gradually accumulates, so that maximum levels (as shown by kidney and liver content) are reached in the fourth and fifth decades.[1] Thereafter, the body burden decreases, and this decrease has never been explained. Smoking is fairly constant during early and middle adult life [8] (between the ages of 25 and 40, about 60% of males smoke). Above this age, however, smoking habits tend to change in that many individuals stop and others reduce the number of cigarettes they smoke (it has been estimated that only 20% of males over the age of 65 years smoke). A fall in cadmium intake brought about by a reduced cigarette consumption might account for the fall in the body burden of cadmium seen in later life.

Our results do not exclude the possibility that cadmium also accumulates with age as the result of dietary ingestion. But if this is the case, it is likely to be of less importance than hitherto thought. The evidence for this, however, will not be forthcoming until an examination is made of cadmium accumulation with age in a population that is exclusively non-smoking.

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