

Key messages

- An almost twofold difference in lung cancer incidence between people living in Copenhagen and in rural areas of Denmark was seen in the 1980s
- This cohort study of the national population shows that smoking explained about 60% of the excess lung cancer risk in Copenhagen for men and 90% for women
- After control for smoking, however, workers had double the cancer risk of teachers or academics, whereas there was only a small independent effect of region
- The outdoor air in Copenhagen around 1970 contained on average 50-80 $\mu\text{g}/\text{m}^3$ of sulphur dioxide, 80-100 $\mu\text{g}/\text{m}^3$ total suspended particulate matter, and up to 10 ng/m^3 benzo(a)pyrene and had peak values of daily smoke of 120 $\mu\text{g}/\text{m}^3$
- The fact that only a small effect of region on lung cancer incidence was seen in the present study indicates that an influence of outdoor air pollution on lung cancer is identifiable only above this pollution level

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Appendix A

Interactions in tobacco consumption models

Some interactions were included in the models when the smoking percentages were estimated. The main dif-

ferences for men were that fewer men aged 30-39 in one family houses or working as other employees smoked than would be expected from the main effects model described in table 2. More young unskilled workers smoked, as did the oldest (50-64) other employees, highly educated employees, and other self employed men. More than expected of the young unskilled workers and highly educated employees in the oldest age group were heavy smokers. Married unskilled workers, unmarried skilled workers, and previously married highly educated employees were heavy smokers more often than expected, while fewer unmarried highly educated employees were heavy smokers. For economically active women, more middle aged (40-49) women in the capital, young women in rural areas, and unmarried highly educated employees smoked than expected. Fewer unmarried female farmers and other self employed women and more unmarried highly educated employees were heavy smokers.

Appendix B

Calculation of smoking risk score

The likelihood curve found when trying to estimate the values for the relative risk for moderate and heavy smoking had a flat top with estimates clearly above 1 and with a proportion of 1 to 3 between moderate and heavy smoker. This flatness is probably due to a systematic variation between cells in the risk factors of smoking on which we have no information, such as type of tobacco, inhalation pattern, and age at start smoking. Therefore we calculated a smoking risk score for each cell using the following formula:

$$\text{smoking risk score} = 1 \times \% \text{ non-smokers} + 5 \times \% \text{ moderate smokers} + 15 \times \% \text{ heavy smokers}$$

The relative risk values of 1, 5, and 15 for non-smokers, moderate smokers, and heavy smokers, respectively, were chosen after consulting the literature.³ The score was calculated for each cell of the study population formed by combinations of risk factors for lung cancer and based on the estimated tobacco consumption in each cell. Values of 3 and 10 could also have been chosen with only minor effects on the estimates for the other risk factors of lung cancer presented in table 3.

Case-control study of evening melatonin concentration in primary insomnia

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The function of melatonin is not fully established, but recent studies suggest that it plays a role in the regulation of sleep. Thus, physiological doses of melatonin given to healthy volunteers decreased the time taken to fall asleep,¹ and the incidence of insomnia in the population rises during middle and old age,² when serum concentrations of melatonin decline.³ Haimov *et al* found that elderly patients with insomnia had lower than normal peak urinary concentrations of the melatonin metabolite 6-sulphatoxy melatonin and a delayed onset to peak secretion.⁴ We investigated evening plasma melatonin concentrations in subjects with primary insomnia and matched controls and predicted that the subjects with insomnia would have lower melatonin concentrations.

Subjects, methods, and results

Cases and controls were recruited predominantly by advertisement, but two cases were referrals from general

practice. The 10 men and 10 women with insomnia had a mean age of 53.9 years (range 40-68), and the 20 controls matched for sex and age (within five years) had a mean age of 54.7 (40-69). The cases and controls were recruited continuously over two years, and all but three of the controls were studied within three months of their matched case. We used a supplemented structured interview to ensure that the cases met criteria for primary insomnia according to *Diagnostic and Statistical Manual of Mental Disorders*, third edition, revised (DSM-III-R). Their mean duration of insomnia was 18 years (range 2-50), and they had no other current axis 1 disorder according to DSM-III-R. The controls had no current axis 1 disorder. None of the subjects had taken psychotropic drugs or β adrenoceptor antagonists for at least one month, and all gave their informed consent to the study, which was approved by the local ethics committee.

Subjects came to the laboratory at 6 pm, when we inserted an indwelling venous cannula under dim light

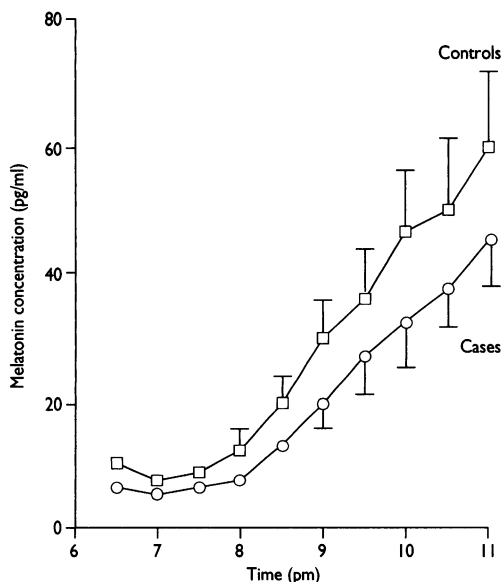


Fig 1—Geometric mean (SD) plasma melatonin concentrations in 20 cases with primary insomnia and 20 matched controls. Cases had significantly lower concentrations than controls ($P=0.028$, analysis of variance of log transformed data)

conditions (<100 lux). Sampling for plasma melatonin began at 6 30 pm and continued at 30 minute intervals until 11 pm. We measured melatonin concentration by means of a radioimmunoassay with a limit of detection of 1.3 pg/ml (intra-assay and interassay coefficients of variation, 8% and 13% respectively). We log transformed the melatonin concentrations to achieve a normal distribution and analysed them with a matched pairs analysis of variance with time and diagnosis as the main factors.

Figure 1 shows the plasma melatonin concentrations. The analysis showed significant differences for diagnosis ($F=5.65$, $df=1.19$, $P=0.028$) and time ($F=113.56$, $df=9.171$, $P=0.001$) but no interaction of diagnosis by

time ($F=0.24$, $df=9.171$, $P=0.987$). For all the time points considered together, the geometric mean paired difference in melatonin secretion between cases and controls was 11.6 pg/ml (95% confidence interval 0.06 to 23.2, $t=2.1$, $df=19$, $P<0.05$).

Comment

Our findings add to data suggesting that some patients with insomnia have decreased melatonin secretion.⁴ We did not sample the subjects up to the usual time of peak melatonin secretion (about 3 am) and therefore cannot tell whether those with insomnia had a phase shift in melatonin secretion with a delayed peak or an overall lowering of melatonin output.

Two further caveats are important. Firstly, people with primary insomnia often experience anxiety and depression; accordingly, lowered plasma melatonin could be associated with the presence of minor psychiatric symptoms rather than insomnia itself. Secondly, it would have been preferable to study the cases and controls simultaneously because this would have avoided possible bias due to seasonal variation in melatonin secretion. Nevertheless, our findings support the possibility that some patients with insomnia may benefit from treatment with exogenous melatonin,⁵ but controlled studies are needed to assess the nature and durability of such an effect.

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Conflict of interest: None.

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THE TEACHER WHO INFLUENCED ME

The importance of communication

It is 1956. The limousine draws up before the portico of Guy's Hospital and out steps Dr Arthur Henry Douthwaite, senior physician to Guy's Hospital, in full morning dress and bowler hat. Waiting to greet him at the top of the steps are the sister, senior registrar, junior registrar, senior house physician, assistant house physician, senior students on the firm, and junior students—one of them me.

We proceed to the ward gravely and by the time we reach the first bed the crowd has swelled threefold as others join voluntarily to gather wisdom. At each bed the grand round takes its usual pattern. The unusual part is that Dr Douthwaite speaks to each patient about his medical problems lucidly but in language the local residents understand.

One day he asks the house physician, "What can we do to help Mr Jones?" The house physician has no idea but suggests, "We could try him on Mist Probono Publico Cum Asafoetida, Sir?" or something like. "Sister, a bottle of Mist Probono Publico," orders Dr Douthwaite, and Sister sends the message down the hierarchy of her minions and the bottle appears. Dr Douthwaite requests that first the house physician and then every person on the round should taste the medicine. Mr Jones is spared and another lesson is learnt.

Dr Douthwaite was a great physician and textbook writer. An expert on drugs, he dissuaded the Home Office from banning heroin for medical use, for which we must still give thanks. Unfortunately, he made one of his rare errors all too publicly at the John Bodkin Adams trial, where his evidence was crucial in securing the acquittal of that genial general practitioner, whose rich patients bequeathed him generous legacies. Legend had it that that cost him the presidency of the Royal College of Physicians. Legend also had it that Dr Douthwaite walked into the casualty department in his usual morning dress and greeted the casualty officer, "I am Arthur Henry Douthwaite and I have just perforated my duodenal ulcer, please arrange my admission." He had.

He was a great man. He taught me that the truly great man cares for his patients and communicates with them. It is a lesson not yet learnt by some great men but it has served one humble general practitioner well.—ANTHONY ABRAHAMS is a general practitioner in Oxford

We welcome filler articles of up to 600 words on topics such as *A memorable patient*, *A paper that changed my practice*, *My most unfortunate mistake*, or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk.