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LETTERS

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Musicians playing wind instruments and risk of lung cancer: is there an association?

Lung cancer is an important public health problem. Tobacco is its main risk factor. Occupation is also an important risk factor. Some jobs have shown higher risks than others, but few investigations have asked about activities or hobbies in leisure time[1] in relation to the risk of lung cancer.

A case-control study was performed between 1999 and 2000 in the Santiago de Compostela Health District (Galicia, northwest Spain). A total of 132 cases with confirmed diagnosis of lung cancer and 187 controls were enrolled. Controls underwent trivial surgery at the same hospital as did the cases. A personal interview about lifestyle and activities (past and present) was conducted by a trained researcher.

We found that, besides tobacco and occupational exposure to carcinogens, some leisure time activities were risk factors for lung cancer.[1] Among the cases there were two musicians who played wind instruments, whereas there were no wind instrument players among the controls. The two cases had been playing the clarinet and trombone for 35 and 30 years respectively. Both were ex-smokers (moderate smokers) and played music as a hobby. They had epidermoid lung cancer and were diagnosed at 57 and 76 years of age.

Since in our population the prevalence of persons playing musical instruments and specifically wind instruments is extremely low, we think that this activity might be a risk factor in development of lung cancer. The very low number of persons playing this type of musical instrument is probably a reason for the lack of studies focused on this activity, as many occupational studies of lung cancer and occupation are based on registries of workers. One study[2] found an increased mortality rate of lung cancer for a category that included painters, potters, musicians, and actors—an inhomogeneous category that did not allow us to extrapolate results. The results were not adjusted according to smoking history.

This hobby requires inspiration and breathing of large volumes of air, making the lung alveoli expand more than in other people. This fact could facilitate the penetrance of carcinogens in the cells of the lung epithelium, and this could be more harmful in smokers. We have found no other studies that have reported this possible association. It would therefore be necessary to explore this association in greater samples of professionally exposed persons in order to ascertain whether this finding is consistent or due to chance.

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How important is personal exposure assessment in the epidemiology of air pollutants?

The paper by Harrison and colleagues[1] and the accompanying editorial by Cherrie[2] in the October 2002 issue of *Occupational and Environmental Medicine* address the important issue of personal exposure assessment (of air pollutants) in environmental epidemiology. After reading both papers we would like to make some comments with regard to the design, conduct and statistical analysis of the study by Harrison *et al* and at the same time answer the question raised by Cherrie in his editorial.

Coming from the occupational exposure assessment arena it is interesting to see that our environmental colleagues are still relying to a large extent on static (microenvironmental) sampling and even rely on shadowing to represent personal exposure. The latter brought back memories of old occupational hygiene textbooks with pictures of technicians standing with a sampling probe in the breathing zone of a worker (clearly hindered while carrying out his work task). It is interesting to note that Dr Cherrie's very relevant earlier work[3] on whether wearing sampling pumps affects exposure (it hardly did) was not mentioned in both papers.

The paper by Harrison and colleagues[1] clearly states as one of its goals to answer the question "Does modelling through the use of microenvironment measurements and activity diaries produce reliable estimates of personal exposure to air pollutants". However, in the only setting where personal exposures were actually measured (phase 1, volunteers; with regard to phase 2 we do not think that shadowing results can be seen as equivalent to personally measured exposure) it is hard to grasp from both fig 1 and table 2 which exposure was actually modelled (1 hour averages, 2–3 day averages) and how (a formula was only provided for measurements within the susceptible groups).

When comparing direct personal measurements for CO and PM_{10} with the modelled results, the authors exclude all data which are not directly comparable—that is, when the volunteer spent most of their time out of house, and all the data for smokers. It is therefore not surprising that good correlations were found between personal and static measurement results. Why were smokers excluded? Was their measured CO exposure representing a different kind of CO leading to a different health effect? We know that excluding smokers or people with unventilated gas heaters is common practice in the statistical analyses of environmental exposures, but this would only make sense if we were expecting different risks from the same exposure originating from different sources.

In fig 1 the authors present 120 comparable data points for 11 individuals; given the repeated nature of the sampling these data points cannot be seen as statistically independent. Putting a simple regression line through these points is therefore not correct and application of a mixed effects model would have been more appropriate. Besides that, when estimating environmental exposure, for instance, for a panel study, we are interested in the full range of exposures both in the temporal and spatial sense (not only for the room with the static sampler). However, Harrison *et al* conclude, "... modelled personal exposure is unable to reflect the variability of measured personal exposures occasioned by the spread of concentrations within given microenvironments".

Both Cherrie and Harrison *et al* claim that microenvironmental sampling would be a good alternative for direct personal exposure measurements that supposedly are "costly and time consuming". However, the costs for sampling microenvironments in a general population study will be far greater if we want to measure all the microenvironments people end up in (for instance, in table 1 seven environments are indicated, and most of them will most likely be different for each study participant). In addition, it will be practically impossible to measure some of these environments as the authors point out. In their study, it was not possible to collect data for all appropriate microenvironments, even for a comparatively small number of subjects.

Recently, a very insightful paper was presented at the X2001 conference in Gothenburg. Seixas and colleagues[4] showed that in a study to assess occupational noise exposure, a task based methodology (analogous to microenvironmental sampling in environmental exposure assessment) could only account for 30% of variability in daily exposures. They even considered this estimate somewhat optimistic since their estimated noise exposures were derived from the same data on which the daily average exposures were estimated. In addition they clearly pointed out that using simple task based averages that artificially compress exposure variability resulted in a very substantial negative bias in the estimated daily exposure.

In our opinion, we should aim to collect personal exposure measurements when estimating exposure for epidemiological studies.

We agree that smaller and lighter sampling instruments will need to be developed, as was suggested by Cherrie in his editorial. Recent studies in both the occupational and environmental arenas have shown that study subjects are capable of carrying out personal measurements themselves (and by doing so, cutting out the costs of the technician).[5–9] In all these studies except one,[7] far more than 100 personal measurements were generated, which shows that studies of this size are not exceptional as was suggested in the editorial by Cherrie.

The question raised by Cherrie, "How important is personal exposure assessment in the epidemiology of air pollution?", can only be answered with a firm "very important", if we want to capture the full range of personal exposures experienced in the general environment. In addition, given the relatively low concentrations in the general environment, we will need to measure these accurately. Microenvironmental monitoring and consequent modelling based on diaries will not provide sufficient resolution and accuracy.

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Will sewage workers with endotoxin related symptoms have the benefit of reduced lung cancer?

Thorn and colleagues[1] reported that sewage workers suffer from various symptoms which can be related to bacterial endotoxin (lipopolysaccharide) exposure. Other studies[2–5] have shown that some members of this occupational group are commonly exposed to endotoxin. However, there appears to be a large discrepancy in endotoxin exposure among those categorised within this group.[2] Endotoxin exposure to some of these workers appears to be sufficient to induce a respiratory response characteristically associated with endotoxin.[2] Workers that have the highest exposure in sewage treatment are suggested to be associated with the waste treatment process.[3] Professor Rylander pointed out that endotoxin exposure to this occupational group is low overall (personal communication with Professor Rylander). Rapiti and colleagues[6] suggested that the lack of an increased lung cancer rate in one study[7] and reduced risk of lung cancer in another[8] for sewage workers may be related to endotoxins in their occupational environment as was originally reported for cotton textile workers.[9] Other studies[10 11] that reported on lung cancer rates for sewage workers support these findings as suggested by Rapiti and colleagues.[6] Rylander[12] and Lange[13] previously reviewed the epidemiological literature on reduced cancer rates in various occupations that are exposed to endotoxin.

A number of epidemiological,[12–16] experimental,[17 18] and clinical[19 20] studies have suggested that endotoxin is effective against cancer. A recent study in humans by Palmberg and colleagues[21] reported that there is a rapid blood response of total leucocytes, monocytes, and granulocytes within seven hours followed by a dramatic decline within 24 hours. These findings are supported by an investigation by O'Grady and colleagues[22] in humans, in which endotoxin was instilled into a lung segment; increased tumour necrosis factor (TNF) and interleukin 1 were found in the bronchoalveolar lavage fluid 2–6 hours afterwards. Cytokine levels returned to normal concentrations within 24–48 hours after treatment. An increase of TNF in lung fluids as a result of exposure to endotoxin and dust containing endotoxin has been reported by others conducting human investigations as well,[23 24] including the suggestion of a dose-response relation.[25] Thus, periodic exposure as would likely be experienced by those in sewage and dusty occupations may afford a continual or pulse stimulation of the immune system. Such stimulation may enhance production of anticancer mediator factors and cells[26] that are suggested to be responsible for observed reduced lung cancer rates.[13]

Experimental studies[27] have suggested that benefit of endotoxin exposure is most effective during initiation of lung cancer with a finding of less benefit for established tumours. This, together with results from Palmberg and colleagues,[21] supports the hypothesis[14 27] that endotoxin in an occupational setting is effective against the early formation of lung cancer. This further suggests that endotoxin reduces the incidence of lung cancer by stimulating the immune system to guard against early lung cancer events.

Additional studies are warranted on the relation of endotoxin and reduced lung cancer rates. This relation has been suggested for textile and agricultural workers.[12–16] There is no reason to believe that it will not exist for other occupational groups exposed to endotoxin. Many have explained that the relation is not one of benefit, but rather methodology and bias, including differences in smoking rates.[6–9] However, this explanation is not supported by experimental and clinical investigations involving endotoxin. The major influence on lung cancer is tobacco use (smoking). Although smoking is identified as one of the reasons for lower than expected rates in some populations, some studies[6–9] have shown that smoking is not always an explainable factor or bias for reduced lung cancer. For example, Rapiti and colleagues[6] reported that the consumption of cigarettes and prevalence of smoking in a population of municipal waste workers was higher than the general population, but the incidence of cancer deaths (standardised mortality ratio) for lung cancer in this group was 0.55. Epidemiological studies need to include and report not only detrimental outcomes but also potentially beneficial associations.

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