LETTERS TO THE EDITOR

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Dear Sir

In the ‘Monitor’ summary article regarding uncertainty in employment in the February 2003 issue of the journal, the conclusion is drawn that this does not result in poorer health than in those in secure employment. I submit that this is most likely to be due to the fact that those affected cannot afford to appear to be sickly by taking time off, as this is likely to put their ‘uncertain’ employment into jeopardy, while those in secure jobs feel that they can afford the luxury of being ill!

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Occupational exposure to methyl tertiary butyl ether: a risk to be assessed

Dear Sir,

Methyl tertiary butyl ether (MTBE) is an oxygenate that is added to gasoline to reduce engine knocking, and to minimize the level of carbon monoxide (CO) and aromatic hydrocarbons in automobile exhausts.

Although used for gasoline blending in Italy since 1973, utilization of this additive has only become widespread in the last decade. In 1990, the US Clear Air Act amendments required oxygenates to be used in gasoline in 39 states in order to reduce automobile CO emissions, particularly high during the winter months. MTBE has therefore become the motor vehicle fuel oxygenate most commonly used in the USA, where it is present in up to 15% v/v. Since the introduction of Directive 98/70/EC, which permits gasoline to contain up to 15% v/v MTBE, this oxygenate has also been more widely used in Europe.

The increasingly widespread use of this oxygenate has caused a large number of workers engaged in automobile refuelling and servicing operations to be exposed to MTBE. Other categories of workers exposed to urban pollution, such as traffic wardens, rubbish collectors and transport drivers, are also exposed to this substance, albeit to a lesser degree.

Several experimental and epidemiological studies have been carried out on MTBE toxicity. Some studies have concentrated on investigating its possible carcinogenic effects.

Evidence from three separate bioassay studies on mice and two different species of rats have shown that chronic exposure to MTBE by inhalation and oral route can cause tumours in animals. However, some disagreement exists in the data currently available in the literature. In fact, Belpoggi et al. [1,2] have reported that oral administration of MBTE led to increased incidence of leukaemia and lymphomas in female rats, and testicular tumours in male rats. Moreover, Bird et al. [3] reported that, in male rats, exposure to MTBE vapours causes an increased incidence of renal tubular-cell tumours and a larger number of testicular tumours. The same study also demonstrated that exposure to MTBE leads to the onset of liver tumours in CD-1 mice.

In contrast, other authors [4,5] have reported that doses similar to those used by Belpoggi et al. [1,2] and Bird et al. [3] did not result in the onset of tumours in the same type of animal models.

In one of our studies [6], we found that in vitro MTBE was able to induce transformation of C3H/10T1/2Cl8 mouse embryo fibroblasts at two different concentrations in the medium (0.336 and 0.672 mM).

The International Agency for Research on Cancer [7] has established that MTBE is not classifiable as to its carcinogenicity to humans (Group 3), because there is limited evidence of this action in experimental animals and inadequate evidence in humans.

In fact, MTBE was classified as a non-cancerogenous substance because in the aforementioned in vivo studies, the incidence of tumours could not be calculated on account of the absence of a mortality-adjusted analysis, sometimes due to incomplete histopathological examination, and because an unusual dosing schedule was used in experiments involving the oral administration of MBTE. Moreover, the animals were allowed to live out their natural lifespan [7].

Furthermore, the US National Toxicology Program’s Board of Scientific Counsellors upheld the decision to place MTBE among non-carcinogenic substances, thus rejecting an attempt to list this chemical as ‘reasonably anticipated to be a human carcinogen’. Mehlman [8] was highly critical of this decision since he claimed that it was contrary to rules and procedures previously set up by the
National Toxicology Program for evaluating the carcinogenicity of chemical compounds.

The state of the art requires further research to be performed on laboratory animals to ascertain whether tumors appear at doses lower than those hitherto tested, and at the same time to study any underlying mechanisms. The study recently published by De Peyster et al. [9] undoubtedly fills these requirements.

With regard to occupational exposure, both MTBE vapours and a biological exposure indicator should be monitored so that long-term effects can be related to exposure. In this case, it would be useful to remember that unmodified MTBE can be measured in exhaled air, blood and urine [10], and that its metabolites, formaldehyde and tert-butanol, can be also determined [11]. Finally, studies to validate the most adequate biological indicator of MTBE exposure need to be undertaken.

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References

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Dear Sir

I was very interested to read the case report on the shift worker who had elevated salivary cortisol due to sleep deprivation [1]. I would like to bring your attention to a study by Meerlo et al. [2] that showed not only is the hypothalamo-pituitary-adrenal (HPA) axis activated by sleep deprivation, but also that the subsequent response to stress is heightened. This could cause a number of effects on shift workers, who probably experience many day-to-day stressors in modern society. Meerlo's study demonstrated that after 48 h of total sleep deprivation, adrenocorticotropic hormone (ACTH) and corticosterone levels were increased, and following a 4 h recovery period, the subsequent response to stress was weakened. A second experiment investigated chronic sleep deprivation, and showed that after 20 h without sleep, ACTH and corticosterone were significantly elevated. Chronic sleep deprivation after 1 day did not affect the subsequent response to stressors but did have an effect after 8 days. These results show that even though cortisol levels had returned to baseline following a recovery period, the HPA response to stressors is affected, reiterating the harmful effects of long-term sleep deprivation.

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References