Toluene diisocyanate induced asthma: outcome according to persistence or cessation of exposure

Sir,—We read with interest the article by Pisati et al (1993;50:60-4) regarding outcome according to persistence or cessation of exposure to toluene diisocyanate. In a recent analysis of asthma compensation claims in Ontario, we have also found (data submitted for publication), as have some of the other reports referenced by Pisati et al, that duration of symptoms before leaving exposure and initial pulmonary function measures were important predictors of outcome.

In explaining the poor state of group A who were still exposed, is it possible that Pisati et al could further sort out the role of continued exposure to toluene diisocyanate vs the initial circumstances such as long duration of exposure and long duration of symptoms before diagnosis? In particular, among the non-improved subjects within group B (subgroup III) who were no longer exposed, the baseline PD_{15} of 424 was similar to that among group A who were still exposed (425). Moreover, as the authors point out, subgroup III had a long mean duration of exposure (15-9 years), and mean duration of symptoms before diagnosis (5-4 years), again similar to those among group A (25 and 6-3 years, respectively). The baseline FEV_{1} was somewhat lower, however, among group A than subgroup III (86-8% vs 94%).

The authors indicated that it was not possible to analyse group A in this way (because no subjects recovered). Whereas removal from exposure is probably the only effective way of preventing deterioration, it would be of interest if the authors could look at subgroups or examine the relative importance of duration of exposure and symptoms before diagnosis vs persistent exposure as predictors of outcome in comparing group A and subgroup III, as they were similar at baseline.

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Authors’ reply
We are grateful for the opportunity to reply to the letter from Liss and Tarlo and thank them for their interesting comments on our paper.

Within group A (patients who had carried on working exposed to toluene diisocyanate), the 13 subjects who had deteriorated after five years of further exposure and the four subjects who were found stable had similar duration of exposure to toluene diisocyanate and symptoms before diagnosis, as well as baseline lung function tests, PD_{15}, methacholine, and severity of bronchoconstriction induced by the toluene diisocyanate inhalation challenge. Therefore, it was not possible to predict what factors affect the different outcome of these toluene diisocyanate asthmatic subjects on persistence of exposure.

As Liss and Tarlo suggested, we compared group A and group III (non-improved subjects within group B, who had stopped exposure) at the time of diagnosis and at the follow up visit. At diagnosis, several clinical and functional indices of the two groups (symptom score, medication score, FEV_{1}, PD_{15}, methacholine, and duration of symptoms before diagnosis) were similar. At follow up, group A was significantly more symptomatic (p = 0.01 by unpaired t test) and required more medication (p = 0.005) than group III (table). Because at diagnosis, however, the mean duration of exposure to toluene diisocyanate of group A was significantly longer than that of group III (25 vs 15-9 years; p = 0.007 by unpaired t test), comparing the two groups of patients is of no use in further sorting out the role of persistence of exposure vs the mean duration of exposure to toluene diisocyanate before diagnosis.


Semen quality in welders exposed to radiant heat

Sir,—The report by Bonde (1992;49:5-10) further illuminates the issue of radiant heat as a reproductive risk for men who weld. It calls to mind an earlier concern of ours over similar risks to reproduction from convective heat exposures among divers who inhabit hyperbaric chambers for long periods. These chambers are pressurised to 30–60 times normal atmospheric pressure. The breathing medium is nearly pure helium with just enough oxygen to maintain a physiological content of oxygen in alveolar gas and arterial blood. Because helium thus compressed has a heat capacity equal to that of water, it is necessary to provide an ambient temperature around 32°C to insure thermal comfort and homeostasis.1 2

Such high ambient temperatures are maintained for many days, because decompression proceeds at only 100

Clinical details of the 17 subjects with persistent exposure to toluene diisocyanate and the 21 non-improved no longer exposed subjects, at the time of diagnosis and at follow up

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group A (n = 17)</th>
<th>Group III (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Still exposed</td>
<td>Non-improved, no longer exposed</td>
</tr>
<tr>
<td></td>
<td>mean (SD)</td>
<td>mean (SD)</td>
</tr>
<tr>
<td>Symptom score:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At diagnosis</td>
<td>1.7 (0.8)</td>
<td>1.9 (0.9)</td>
</tr>
<tr>
<td>At follow up</td>
<td>2.3 (1.1)†</td>
<td>1.5 (0.7)</td>
</tr>
<tr>
<td>Medication score:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At diagnosis</td>
<td>1.4 (1)</td>
<td>1.2 (0.6)</td>
</tr>
<tr>
<td>At follow up</td>
<td>2.8 (1)**†††</td>
<td>1.6 (1.4)</td>
</tr>
<tr>
<td>FEV_{1}, (% predicted):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At diagnosis</td>
<td>86.8 (22.5)</td>
<td>94 (17.7)</td>
</tr>
<tr>
<td>At follow up</td>
<td>72.9 (19.4)††</td>
<td>82.7 (29)</td>
</tr>
<tr>
<td>FVC/VC (%):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At diagnosis</td>
<td>66.4 (11.7)</td>
<td>71.4 (11.3)</td>
</tr>
<tr>
<td>At follow up</td>
<td>60.1 (13.5)†</td>
<td>68.5 (14.5)</td>
</tr>
<tr>
<td>PD_{15}, methacholine (µg):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At diagnosis</td>
<td>425 (608)</td>
<td>424 (304)</td>
</tr>
<tr>
<td>At follow up</td>
<td>301 (610)†††</td>
<td>501 (571)</td>
</tr>
</tbody>
</table>

* p = 0.01; ** p = 0.005 (unpaired t test between groups).
†† p < 0.01; ††† p < 0.005; †††† p < 0.001 (paired t test between initial and follow up examination).
ft/day (about 3 atmospheres/day) so as to minimise the risk of decompression sickness.

Our measurements relevant to the study of Bonde were limited to scrotal skin temperatures, which were consistently higher in hyperbaric helium than in air at sea level (35.9 °C vs 34.6 °C, p < 0.05). Scrotal temperature rose another 0.3 °C during a series of two-hour thermal balance observations of two resting divers, over the first two weeks of decompression. The sum of these increases is close to that reported by Bonde, but the prolonged nature of the hyperbaric helium exposures raises further questions. Firstly, would the higher scrotal temperatures in such divers be attended by more major disturbances in spermatogenesis? If so, what would be the time course of recovery? As far as I am aware these questions have not been considered directly in human subjects. Because rats and mice require even higher ambient temperatures for thermal homeostasis in such atmospheres, their study might provide valuable clues.3 Bonde’s work is a reminder that such issues remain unresolved and are a challenge to diving physiology and reproductive biology in general.

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NOTICES

**Symposium on health hazards of glycol ethers. 19-21 April 1994, Abbaye de Pont-à-Mousson, Nancy, France.**

Glycol ethers are a family of products largely used as industrial chemicals and also in consumer products (paints, inks, varnishes, cleaning agents, cosmetics). New research data on their potential carcinogenic and genotoxic characteristics highlight the concern for the control of the potential toxic hazards involved. The purpose of this symposium is to provide a scientific basis for risk assessment and management.

The scientific programme will consist of invited lectures, free communications, and poster sessions. Ample time will be reserved for discussion. The working languages will be English and French and simultaneous translation will be provided.

Topics will include occupational and domestic exposure, toxicokinetics, metabolism, biomonitoring, mechanisms of action, in vivo and in vitro toxicity studies, effects on humans (case reports, epidemiological studies), risk assessment.

The organisers are the National Institute for Safety Research, France (INRS), the National Institute for Occupational Safety and Health, USA (NIOSH), and the National Institute for Occupational Health, Sweden (NIOH).

For further information contact the Symposium Secretariat, International Symposium on Health Hazards of Glycol Ethers, INRS Avenue de Bourgogne BP27, F 54 501 Vandouvre Cédex France. Tel (33) 83 50 20 27, Fax (33) 83 50 20 96.

**Work with display units: fourth international scientific conference. 2-5 October 1994, Aula Magna, University of Milan, Italy.**

Topics will include risk assessment, medical surveillance, stress factors, visual problems, musculoskeletal disorders, skin problems, pregnancy and VDU work, health information and education, new VDU applications, mobile and home use, participation of user, unions, and institutions, environmental conditions, furniture requirements, equipment, new techniques, workplace design, international legislation and national policies, application of EEC Directive 90/L70 in different countries, and harmonisation between legislation and standards.

The official conference language is English.

For further information contact the Organising Secretariat Work with Display Units, AES Congressi S.r.l., 20139 Milan-Via Schiavilla, 1, Italy. Tel +39(2) 5510523; Fax +39(2) 57400473.
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