Notes and miscellanea

Do amines induce occupational asthma in workers manufacturing polyurethane foams?

A number of amines have been described as causing occupational asthma.¹⁻⁶ Recently, Belin and his coworkers suggested that amines, particularly of N-methylmorpholine, might be causative agents in the development of bronchial hyperreactivity in workers manufacturing polyurethanes from isocyanates.⁷ We studied this problem in 1974,⁸ focusing particularly on toluendiamine (TDA) which is formed when toluendiisocyanate (TDI) comes into contact with water; it is also formed during the chemical processes by which polyurethane foams are produced (fig).

We considered that this TDA might play a part in inducing occupational asthma, and in order to evaluate this possibility 12 subjects occupationally exposed to polyurethane foams and complaining of symptoms of wheezing and breathlessness at work were submitted to a bronchial provocation test with methacholine, TDI, and TDA.

The methacholine test was carried out by administering doses in the range 20–2000 µg by a dosimeter (MEFAR), thus establishing a dose-response curve.⁹ Sensitivity to methacholine was expressed as the dose of methacholine provoking a 15% fall in

the forced expiratory volume in one second (PD₁₅ FEV₁) measured by means of a bell spirometer (Volumograph). The TDI challenge was performed by exposing the subject for 15 minutes to an atmosphere containing 0.01 ppm of TDI in an inhalation chamber.¹⁰ The test was considered positive when a 15% fall in FEV₁ was found after exposure.

Exposure to TDA was carried out in the same chamber on two different days. The amine concentrations to which the subjects were exposed were: on the first day, 1.31 mg/m³ and on the second day 3.21 mg/m³, being the theoretical concentrations of amine corresponding (through chemical reduction) to atmospheric TDI concentrations of, respectively, 0.07 mg/m³ (0.01 ppm) and 0.14 mg/m³ (0.02 ppm).

The table shows the results of our study. A high sensitivity to methacholine was shown in 10 subjects (PD₁₅ FEV₁ < 1000 mcg); subjects 8 and 9 responded to higher doses of methacholine (1320 and 1840 µg) but lower than the minimum dose (2000 µg) at which the normal subjects respond.

All the subjects had positive reactions to TDI but none responded to TDA.

These data do not support the view that TDA produces asthma in workers exposed to polyurethane foams; the agent which provokes their respiratory symptoms appears to be TDI.

The reactivity of TDI with organic compounds is probably so high and so rapid that the onset of

Production of TDA from TDI during the formation of polyurethane foams.

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Results of bronchial provocation tests

Subject	Methacholine PD ₁₅ FEV ₁ (µg)	Toluendiisocyanate 0.01 ppm	Toluendiamine 1.31 mg/m ³ 3.21 mg/m ³	
		Type of response	Response	
1	132	Late	None	None
2	86	Immediate	None	None
3	220	Immediate	None	None
4	86	Immediate	None	None
5	610	Late	None	None
6	68	Immediate	None	None
7	86	Late	None	None
8	1320	Dual	None	None
9	1840	Late	None	None
10	420	Immediate	None	None
11	520	Late	None	None
12	68	Immediate	None	None

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adverse reaction precedes the biotransformation of isocyanate into amines. It would be interesting, therefore, to perform in vitro studies on the kinetics of the reaction between TDI and organic compounds in the bronchial mucus.

F CANDURA
 GIANNA MOSCATO

*Scuola di specializzazione in Allergologia e
 Medicina del lavoro dell'Università degli Studi di
 Pavia (Direttore: Prof F Candura) Fondazione
 Clinica del Lavoro di Pavia.*

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