

Follow-up study of patients with respiratory disease due to toluene diisocyanate (TDI)

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Summary

The outcome of the respiratory symptoms, pulmonary function tests and bronchial hyperresponsiveness was studied in forty-seven workers with respiratory disease due to toluene diisocyanate (TDI) (twenty-seven asthmatic and twenty non-asthmatic subjects) after about 2 years from the first examination. Eight of twelve asthmatic subjects who left the industry after the first examination complained at the follow-up of dyspnoea and wheezing, but pulmonary function tests were unchanged; bronchial hyperresponsiveness decreased in three, but most were still positive to challenge test with bethanechol at the follow-up. Fifteen subjects who continued their exposure to TDI showed at the follow-up a significant decrease of the spirometric parameters and an increase of the bronchial hyperresponsiveness, and symptoms of chronic bronchitis were more frequent at the second examination. Non-asthmatic subjects, both exposed and non-exposed to TDI at the second examination, showed a significant decrease of the pulmonary function tests but no relevant changes in bronchial hyperresponsiveness. Our data suggest that stopping occupational exposure to TDI frequently did not produce an improvement of the TDI bronchial asthma, and persistence of the occupational exposure causes a more rapid decline in the respiratory function.

Introduction

Toluene diisocyanate (TDI)-induced bronchial asthma is frequent in workers using polyurethane varnish in the furniture industry. Many studies have been performed in attempts to demonstrate the pathogenesis of the disease, but there are very few observations about follow-up of the respiratory symptoms or bronchial hyperresponsiveness in patients with occupational asthma. Innocenti, Franzinelli and Sartorelli (1981) reported the disappearance of dyspnoea and wheezing in thirty-two but a significant decrease of VC and FEV₁ in all thirty-seven TDI asthmatic patients who left the industry after 12 months. Lam, Wong and Chan-Yeung (1979) found a slight

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decrease of non-specific bronchial hyperresponsiveness in four TDI asthmatic patients no longer exposed to TDI.

The outcome of other types of occupational asthma has been described. Chan-Yeung and co-workers (1977, 1982) observed in asthma due to Western Red Cedar: 50% of the patients showed a complete disappearance of the asthmatic symptoms and a decrease of the bronchial hyperresponsiveness, the remaining 50% continued to complain of dyspnoea and wheezing, and their non-specific bronchial hyperresponsiveness was often increased. All patients had left their job and no significant decrease of their spirometric values was observed at 39.6 months.

Similar data are reported by Simonsson *et al.* (1981) in eleven workers with aluminium salt bronchial asthma. Sherwood Burge (1982) in a group of workers with occupational bronchial asthma caused by colophony fumes observed that histamine reactivity had returned to normal in half the workers who had left their original occupation.

In this study we report 2 years follow-up of the respiratory symptoms, spirometric values and non-specific bronchial hyperresponsiveness of forty-seven workers in the furniture manufacturing industry with respiratory disease due to TDI.

Patients and methods

Patients

Forty-seven workers in the furniture manufacturing industry exposed to TDI were recalled for follow-up examination. At the first examination all patients were submitted to respiratory function tests, allergologic evaluation and bronchial challenge tests. The diagnosis of TDI bronchial asthma was made in twenty-seven patients with symptoms of bronchoconstriction by specific bronchial provocative test (sBPT) with polyurethane varnish (asthmatic subjects, group I). Twenty patients related dyspnoea and wheezing or chronic cough and sputum or upper airway complaints, but were not responders to sBPT (non-asthmatic subjects, group II). At the follow-up examination, all the patients were questioned about continuing occupational exposure to TDI and the presence of respiratory symptoms. Spirometric measurements and bronchial non-specific challenge tests were repeated.

Methods

Skin tests: eleven common allergens (inhalants, danders, mites and moulds) were tested using the prick method.

Pulmonary function tests were carried out by means of a Pulmotest Godart spirometer; VC, FEV₁ and FEF₂₅₋₇₅ were measured.

Bronchial hyperresponsiveness was performed as previously described (Parlanti *et al.*, in press); briefly the patient inhaled the solution of bethanechol (5 mg/ml) by means of a Bird Mark 7 nebulizer in IPPB and the number of the breaths was gradually increased up to a maximum of seventy (1 + 4 + 5 + 10 + 10 + 20 + 20). The procedure was stopped when a 15% drop in FEV₁ occurred or in absence of any airway response, when the maximum number of breaths was reached.

Occupational-type sBPT was performed as previously described using polyurethane varnish (Paggiaro *et al.*, in press).

Table 1. Clinical features of the patients at the first examination

	Asthmatics Group I	Non-asthmatics Group II
Number	27	20
Age (years)	50.2 ± 9.6	54.4 ± 6.0
Duration of exposure (years)	15.6 ± 10.5	20.7 ± 8.4*
Male/female	16/11	15/5
Smoking habit		
Smokers	8 (30%)	14 (70%)
Non-smokers	19 (70%)	6 (30%)
Allergy		
Positive skin tests	12 (44%)	3 (15%)
Atopic history	12 (44%)	7 (35%)
Symptoms		
Dyspnoea and wheezing	27 (100%)	11 (55%)
Chronic cough and phlegm	7 (26%)	11 (55%)
Rhinitis	12 (43%)	8 (40%)
Pulmonary function		
VC < 80%	1 (4%)	1 (5%)
FEV ₁ < 80%	5 (15%)	5 (25%)
FEF ₂₅₋₇₅ < 75%	7 (63%)	9 (45%)
Bethanechol inhalation test		
Positive	17 (63%)	7 (35%)
Response to sBPT		
Late	11 (41%)	—
Dual	10 (37%)	—
Immediate	6 (22%)	—

* Significantly different from Group I ($2P < 0.05$).

Results

The clinical features of the patients at the first examination are reported in Table 1. Non-asthmatic patients were slightly older than asthmatic subjects, and showed significantly greater exposure times to TDI (20.7 ± 8.4 and 15.6 ± 10.5 years, respectively). The majority of the asthmatic patients were non-smokers, whereas 70% of the non-asthmatic subjects were smokers. A positive reaction to the common allergens was more frequent in asthmatic than in non-asthmatic patients; the latter showed more frequently chronic cough and phlegm. Most patients in both groups did not have a baseline airway obstruction. Bronchial hyperresponsiveness to bethanechol inhalation test was observed in 63% of asthmatic and in 35% of non-asthmatic subjects. The sBPT showed a late or dual response in twenty-one and an immediate reaction in six subjects.

At the follow-up, twelve of twenty-seven patients with TDI bronchial asthma had left the industry (group Ia) while fifteen continued to be exposed to polyurethane varnish (group Ib); ten non-asthmatic patients ceased exposure to TDI (group IIa) and ten continued their job (group IIb). Clinical details and respiratory symptoms of the patients at the initial and at the follow-up examination are reported in Table 2. Duration of the follow-up was different in the four groups and ranged from 19.0 ± 4.9 months in the group IIb to 35.6 ± 13.8 months in the group IIa. Symptoms of

Table 2. Clinical features of the patients at the first examination and at the follow-up

	Group Ia	Group IIa	Group Ib	Group IIb
Number	12	10	15	10
Age at the diagnosis (years)	52.9 ± 10.0	59.3 ± 3.7	48.1 ± 8.3	50.6 ± 3.3
Duration of exposure (years)	12.8 ± 9.0	19.5 ± 6.7	17.6 ± 10.8	21.9 ± 9.2
Duration of follow-up (months)	25.2 ± 12.1	35.6 ± 13.8	27.1 ± 11.4	19.0 ± 4.9*
Male/female	8/4	9/1	8/7	6/4
Smoking habit				
Smokers	4 (33%)	8 (80%)	4 (27%)	6 (60%)
Non-smokers	8 (67%)	2 (20%)	11 (73%)	4 (40%)
Symptoms				
Dyspnoea and wheezing				
initial	12 (100%)	6 (60%)	15 (100%)	5 (50%)
follow-up	8 (67%)	3 (30%)	14 (93%)	5 (50%)
Chronic cough and phlegma				
initial	5 (43%)	7 (70%)	2 (13%)	4 (40%)
follow-up	5 (43%)	9 (90%)	10 (67%)	4 (40%)

* Significantly lower than Group IIa and Ib ($2P < 0.05$).

bronchoconstriction were less frequent at the follow-up in the subjects who had ceased exposure to TDI, but eight of twelve asthmatic patients (group Ia) continued to complain of dyspnoea and wheezing. Only one patient in group Ib no longer had attacks of bronchoconstriction; this patient had considerably reduced his TDI exposure. At follow-up the prevalence of the symptoms of chronic bronchitis had greatly increased in the group Ib patients.

The results of the pulmonary function tests (expressed as percent of predicted) and bronchial hyperresponsiveness are reported in Table 3. Group Ia patients showed a

Table 3. Pulmonary function tests (as % of predicted) and bronchial hyperresponsiveness of the patients at the first examination and at the follow-up

	Group Ia	Group IIa	Group Ib	Group IIb
Pulmonary function tests				
VC				
initial	95.1 ± 19.5†	103.3 ± 13.9	105.9 ± 12.3	103.4 ± 15.7
follow-up	96.7 ± 20.5	93.7 ± 12.0*	94.4 ± 15.6*	102.2 ± 17.6
FEV ₁				
initial	93.7 ± 21.6	90.3 ± 25.8	100.7 ± 20.1	101.6 ± 24.4
follow-up	96.7 ± 23.2	79.2 ± 19.4*	92.8 ± 18.1*	93.7 ± 20.4*
FEF ₂₅₋₇₅				
initial	73.7 ± 32.0	67.5 ± 24.5	71.3 ± 26.3	79.4 ± 24.0
follow-up	63.8 ± 35.9	52.3 ± 24.2*	56.3 ± 27.0*	67.3 ± 30.9*
Bronchial hyperresponsiveness				
initial	8 (67%)	4 (40%)	9 (60%)	3 (30%)
follow-up	7 (58%)	2 (20%)	11 (73%)	2 (20%)

* Significant difference ($2P < 0.05$) from the initial value.

† Significant difference ($P < 0.05$) from the Group Ib.

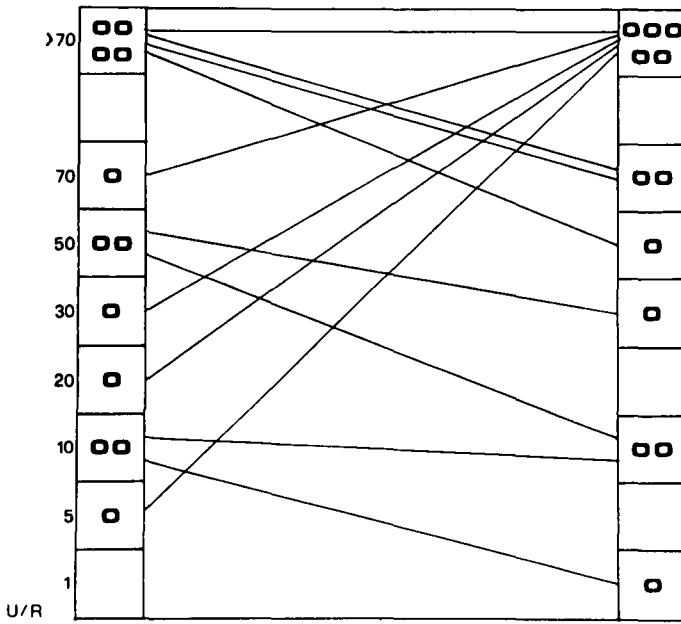


Fig. 1. Bronchial hyperresponsiveness (expressed as U/R of bethanechol) of the Group Ia patients at the first examination and at the follow-up.

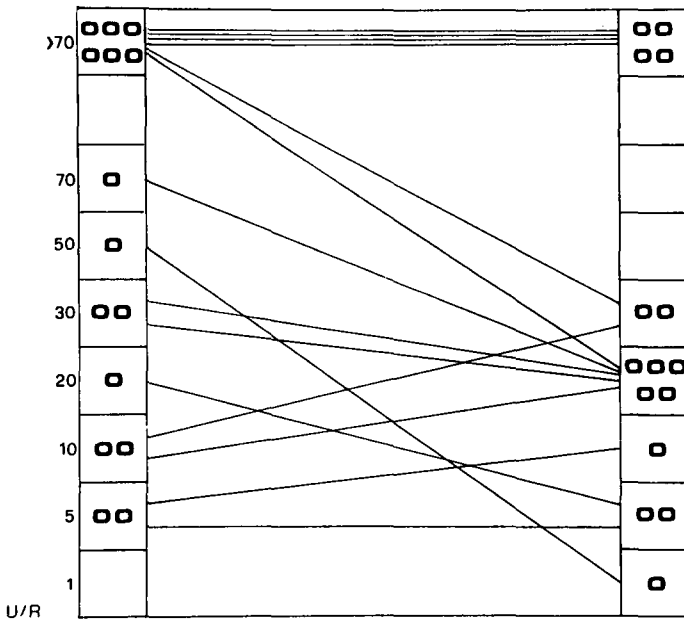


Fig. 2. Bronchial hyperresponsiveness (expressed as U/R of bethanechol) of the Group Ib patients at the first examination and at the follow-up.

slightly reduced baseline VC in respect to the other groups (significantly lower than VC of the group Ib patients), while the patients who had left their job showed a baseline FEV₁ slightly but not significantly lower than the other groups. At the follow-up group Ia patients showed no significant decrease in the spirometric parameters; group IIa and Ib patients showed a significant decrease of the spirometric values, such as group IIb patients as regard as FEV₁ and FEF₂₅₋₇₅.

Bronchial hyperresponsiveness was slightly reduced in the non-asthmatic patients at the follow-up. At this time in the group Ia patients (Fig. 1) four patients became negative to bethanechol inhalation test, while three non-hyperreactive patients who had ended the work became slightly hyperreactive at the follow-up. In the asthmatic patients who had not left the industry, bronchial hyperresponsiveness was generally increased at the second examination (Fig. 2).

Discussion

The clinical course of respiratory disease due to TDI is not known. Previous observations (Innocenti *et al.*, 1981; Lam *et al.*, 1979) suggested that asthmatic symptoms or bronchial hyperresponsiveness decreased when asthmatic patients had left their job. We found that most TDI asthmatic patients who stopped work continued to complain of dyspnoea and wheezing and often showed a persistent bronchial hyperresponsiveness. No correlation was found between the skin sensitivity to common allergens and the persistence of asthmatic symptoms and bronchial hyperresponsiveness. These data are in accord with the findings of Chan-Yeung and co-workers (1977, 1982), Simonsson *et al.* (1981) and Sherwood Burge (1982) suggesting that in many patients the respiratory disease induced by TDI may persist after exposure has ceased. Furthermore bronchial hyperresponsiveness persists and sometimes appears with the progress of the symptoms.

Unlike Chan-Yeung *et al.* (1982) we are unable to correlate the persistence of the symptoms and bronchial hyperresponsiveness after stopping the work to the TDI exposure time or to the type of response to TDI inhalation test. Nevertheless the eight patients with persistent bronchoconstriction showed a slightly greater TDI exposure time and duration of symptoms (14 and 6.9 years, respectively) in respect to the other four patients (10.5 and 5.3 years); moreover their baseline spirometric values were worse at the first examination.

Follow-up study of the asthmatic patients who continued the work confirms previous observations (Innocenti *et al.* 1981; McKerrow, Davies & Parry Jones, 1970; Peters, 1970) about the appearance of symptoms of chronic bronchitis and the worsening of the respiratory function tests. Bronchial hyperresponsiveness was also generally increased.

Non-asthmatic subjects showed at the follow-up a slight change in the bronchial hyperresponsiveness and a significant decrease of the spirometric values. This impairment of the lung function was present also in the subjects who left the work, probably owing to the greater mean age and the higher prevalence of the chronic bronchitis in this group at the first examination, 70% being smokers.

In conclusion, our data suggest that the end of the occupational exposure to TDI frequently did not produce an improvement of the TDI bronchial asthma, but in many cases symptoms of bronchoconstriction and bronchial hyperresponsiveness persist or may get worse. On the other hand, persistence of the occupational exposure causes a more rapid decline of the respiratory function.

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