

ALLERGY TO TETRAMETHYLTHIURAM DISULPHIDE, A COMPONENT OF PESTICIDES AND RUBBER

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Abstract: Since 1970 patch tests have been carried out on 39,420 consecutive patients with contact dermatitis using two rubber accelerators: dimercaptobenzothiazole (2-MBT) and tetramethylthiuram disulphide (TMTD). The second substance is also a component of pesticides. Over the years, the incidence of sensitivity to these substances was similar. But in the recent years the incidence of TMTD sensitivity began rising. This fact is explained by more frequent use of rubber gloves connected with AIDS prophylaxis. Independently of this, it was found that a part of alcoholic patients treated with disulfiram (tetraethylthiuram disulphide) showed a cross-reaction to TMTD.

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The development of industry and introduction of chemicals into everyday life have produced a continuing increase in the incidence of contact dermatitis due to several causes. An important observation is the appearance of sensitivity to ever new chemicals. Another factor is the presence of these allergens in the substances in contact with human skin - an example can be tetramethylthiuram disulphide (TMTD) which is one of the main allergens in rubber, and also a component of pesticides.

The purpose of the present study was to trace the incidence of sensitivity to TMTD in Poland during a period of 25 years.

MATERIALS AND METHODS

The study was carried out on a group of 39,420 consecutive patients tested and treated for dermatitis in the Department of Dermatology, Medical Academy in Warsaw in the years 1970–1996. In all patients patch tests [6] were done with two rubber accelerators: tetramethylthiuram disulphide and dimercaptobenzothiazole (2-MBT). In 40 patients tests with tetraethylthiuram

disulphide (TETD) were additionally conducted. In addition to this, certain patients were also tested with 20 other rubber components, only some of whom produced sensitivity reactions [3]. In all, over 900,000 patch tests were carried out in our laboratory of which only about 10% were associated with rubber or pesticides.

The statistical analysis was carried out using the χ^2 test with Yates' correction for small groups, and Cramer's coefficient correlation for pairs of features, using significance level $p < 0.05$ [4].

RESULTS AND DISCUSSION

Comparison of the prevalence of sensitivity to two rubber accelerators: MBT and TMTD. During the study period, the total number of patients sensitive to rubber components has decreased. Presently precise calculations cannot be carried out since many patients are sensitive to several components of rubber, therefore the sum of all patients sensitive to accelerators, antioxidants and bulking agents would greatly exceed the number of those positive to rubber.

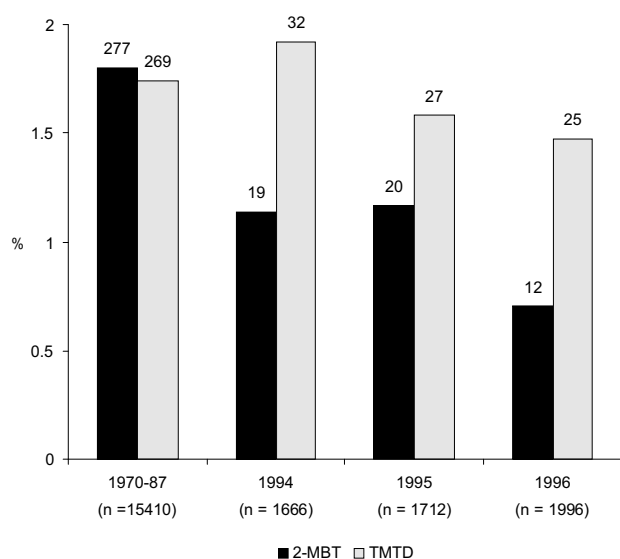


Figure 1. Percent of patients positive to 2-MBT and TMTD in consecutive years. n = number of examined patients. Numbers of positive reactions are shown above the bars.

In relation to both rubber accelerators studied, the following observations were made. The first is that the number of patients positive to each of the two accelerators has decreased. The second observation is that for a long period of time (over 20 years) they were equally frequently the cause of sensitivity, while recently TMTD has become the more frequent allergen than 2-MBT. This is illustrated in Figure 1. In 1996 this difference was higher than in 1995 and has become statistically significant ($p < 0.05$). It seems that lower frequency of contact dermatitis caused by rubber is, at least in part, due to the ever more common use of plastic materials. In the available literature, we found no similar trends, although tetramethylthiuram was reported to sensitise somewhat more frequently than mercaptobenzothiazole (3.8 compared to 3.5%) [1].

The prevalence of sensitivity to TMTD and 2-MBT in males and females. No significant difference related to gender was found in the sensitivity to both rubber accelerators. In certain time periods men were slightly more frequently sensitised, and in other periods the patch tests were more frequently positive in women, but the differences were never statistically significant.

The study of sensitivity to various rubber components carried out in Warsaw in the years 1979–1983 also showed no statistically significant differences in the prevalence of sensitivity to TMTD and 2-MBT between men and women in various occupations. The only exceptions were disulfiram users [3].

Primary allergy to tetraethylthiuram disulphide (TETD, disulfiram) with secondary sensitivity to tetramethylthiuram disulphide (TMTD). TETD (disulfiram, brand name “Anticol” Polfa) is used in the management of selected chronic alcoholics who want to remain in a state of enforced sobriety. Assuming, in view

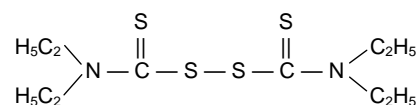


Figure 2. Tetraethylthiuram disulphide (TETD).

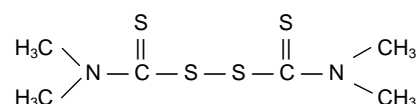


Figure 3. Tetramethylthiuram disulphide (TMTD).

of the high similarity of the chemical structure of TETD (Fig. 2) and TMTD (Fig. 3), and the possibility of cross-reactions between these compounds, we have studied three times in that 25-year period persons exposed to TETD. First, we tested patients with TETD and TMTD in cooperation with a clinic for alcoholics. The study was carried out on 25 patients with poor healing of wounds after disulfiram (“Anticol” Polfa) implantation. None of them was positive to the studied compounds. In the later study, among 12 tested anticol producers we found four persons with primary sensitivity to TETD and secondary cross-reactivity to TMTD. In the same study we also tested eight patients with poorly healed wounds after implantation and in two of them positive results with TETD and TMTD were obtained. The third period of interest in this problem was in the 1990s when six alcoholics with poorly healing implantation wounds were tested. In two men we obtained positive results with TMTD and TETD. In this study, a significant difference between patients positive and negative to these compounds was noted. Positive patch test results were observed only in patients with evident signs of dermatitis at the site of implanting disulfiram.

Allergy to TMTD in health service workers. Recently we observed a significant rise in the prevalence of allergy to TMTD (but not to 2-MBT) related to intolerance to surgical gloves in health service workers. This is believed to be connected with more frequent use of rubber gloves as suggested by instructions for AIDS prevention. This problem is discussed elsewhere [8]. In Table 1, of interest is the observation that earlier (in 1986–1987) in a large group of health service workers with dermatitis no one was positive to TMTD.

It should be remembered that more frequent use of rubber gloves by health service workers presently causes

Table 1. Sensitization of health care workers with dermatitis to TMTD and MBT in consecutive years.

	Physicians			Dentists			Nurses		
	n*	TMTD [†]	2-MBT [†]	n	TMTD	2-MBT	n	TMTD	2-MBT
1986	8	0	0	7	0	0	74	0	0
1987	12	0	0	8	0	0	40	0	0
1994	22	3	0	20	3	0	73	3	0
1995	25	3	1	19	1	1	72	8	3
1996	20	3	1	15	3	1	54	8	1

* number of examined persons; [†] number of positive reactions.

not only contact sensitivity to TMTD but also immediate reactions to latex [2, 9].

Selected cases of sensitivity to TMTD. The study carried out in our outpatient clinic in 1979–1985 showed that occupational sensitivity to TMTD was most frequent in rubber industry workers (4.8%), followed by metallurgic workers and mechanics (4.5%), car drivers (4.2%), chemical industry workers (4.2%) and farmers (4.0%) [5]. In East Germany in the 1970s TMTD was causing relatively frequent sensitivity in workers employed in mechanical cattle slaughtering [10]. A case was reported also of a florist with primary sensitivity to “Sadoplon” (a fungicide containing TMTD) who showed a secondary intolerance to a bicycle tyre which she touched accidentally [7]. Over 25 years, only a few patients came to our clinic with primary sensitivity to

Sadoplon or “Zaprawa nasienna”, a seed dressing containing TMTD. It has not been possible to establish the exact number of these patients, but it was very small. In a group of 12 patients without contact with pesticides but sensitive to TMTD we tested “Sadoplon” and 10 of them were positive.

Thus, the risk of poor tolerance of pesticides containing TMTD is high in all persons who are positive to this compound on patch-testing. Farmers are occupationally exposed to TMTD from two sources: rubber and pesticides.

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