

Mercaptobenzothiazole or the mercapto-mix: which should be in the standard series?

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Mercaptobenzothiazole (MBT) compounds are well known contact allergens. To detect rubber allergic patients we use both MBT (2% in petrolatum) and a mercapto-mix with 4 constituents of 0.5% each in our standard series. In this article the EECDRG presents data of in total 32 475 consecutive tested patients attending the respective contact dermatitis clinics from 11 centres in Europe to determine if the mix and MBT detected the same allergic patients. We found 327 patients positive to the mix or MBT, or to both. 261 were positive to the mix and 254 to MBT. MBT was negative in 73 patients who were positive to the mix. If the mix had not been in the standard series, on average 22% of patients allergic to a mercapto-compound would have been missed, for MBT this would have been on average 20%. All clinics would have missed a significant number of positive reactions if both compounds had not been tested. We conclude, that both the mercapto mix and MBT are required in the standard series.

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Mercaptobenzothiazole compounds are well-known contact allergens. They can be found in rubber products as accelerators but they are also used as antirust agents and fungicides, e.g. in metal working fluids and agricultural pesticides. Mercaptobenzothiazole (MBT) 2% in petrolatum was part of the first 20 standard patch test allergens proposed by the ICDRG (International Contact Dermatitis Research Group) in 1968 (1, 2). In the 1970s MBT was replaced by a mix (3, 4) which consisted of 4 chemicals each in a concentration of 0.25%: 2-mercaptobenzothiazole (MBT), N-cyclohexyl-2-benzothiazyl sulfenamide, 2,2'-dibenzothiazyl disulphide and 2(4-morpholinyl)-mercaptobenzothiazole. Some years later the concentration of each chemical was raised to 0.5% (5). In 1979 the North American Contact Dermatitis Group advised a mercapto-mix without MBT, the concentrations of the 3 remaining 3

constituents were 0.333%. MBT itself was tested in a concentration of 1% in petrolatum; investigations were suggestive that otherwise mercapto-compounds allergic patients were missed (6). In 1988 the ICDRG and the EECDRG recommended adding MBT 2% to the standard series to avoid false negative reactions (7). Hansson & Agrup (1993) (8) reported on the instability of the mercapto-mix substances and as MBT was the stable end-product they proposed using MBT as the single chemical for patch testing for mercaptobenzothiazole/derivatives sensitivity. Shortly afterwards Geier & Gefeller (1995) (9), using data obtained from the Information Network of Departments of Dermatology (IVDK) in Germany, that the mix could be replaced by MBT.

15 years later we are still using MBT in combination with a mix in our standard series.

Even the test concentrations still differ between the American and the European series. The EECDRG recommends MBT 2% and a mix with 4 constituents of 0.5% each, the NACDG advises MBT 1% in combination with the mix with 3 chemicals each 0.333%. For practical reasons, the ICDRG follows the advice of the NACDG (10).

The EECDRG reviewed their results of the European standard series for the years 1996–2000 (11). The results of patch testing about 26 000 patients raised again the question of having both MBT and the mercapto-mix in the standard series as both test preparations were positive in 1% of the tested population. The data from clinics of the EECDRG were used to determine if the mix and MBT detected the same allergic patients.

Patients and Methods

The data was retrospectively compiled for the period 1996 through 2000 from 11 centres in Europe. Included were consecutive tested patients attending the respective contact dermatitis clinics, in total 32 475 patients.

Patch testing was performed according to the ICDRG guidelines with the European Standard series (e.g. MBT 2% and mercapto-mix 2%). The results were based on the final evaluation of the patch testing in each clinic, usually the day 3 or 4 reading. Finn chambers® were used in 8 and Van der Bend Square Chambers® in 2 centres. One centre used the TRUE Test® system.

Results

The data of each clinic is given in Table 1: the total number of patch-tested patients and those who were positive for mercapto-compounds, either the mix or MBT and the number of patient not reacting to one of these two compounds. The quotient of these figures gives the percentage of patients which would not have been identified if the mix or MBT was not included in the European Standard Series. If the mix had not been in the standard series, on average 22% of the patient allergic to a mercapto-compound would have been missed. The variation between the involved clinics ranged between 0% and 34%. This is due to the small numbers of positive reaction in the separate clinics. For MBT this would have been on average 20% if this substance had been omitted (range 0–32%).

The combined figures of the 11 clinics are shown in Table 2. If all figures are added together we have 327 patients positive to the mix or MBT, or to both. 261 were positive to the mix and 254 to MBT. MBT was negative in 73 patients who were positive to the mix.

Table 1. For each clinic is given the number of patients which would not have been traced if the mercapto-mix and mercapto-benzothiazole, respectively, were left out of the European standard series

Clinic	Total											
	1	2	3	4	5	6	7	8	9	10	11	
Not traced patients if												
Mix not in ESS	3/15 (20%)	1/13 (8%)	11/32 (34%)	6/21 (29%)	4/19 (21%)	17/53 (32%)	12/38 (32%)	17/82 (21%)	1/25 (4%)	0/10 (0%)	1/19 (5%)	73/327 (22%)
MBT not in ESS	3/15 (20%)	0/13 (0%)	5/32 (16%)	5/21 (24%)	5/19 (26%)	13/53 (32%)	2/38 (5%)	21/82 (26%)	6/25 (24%)	2/10 (20%)	4/19 (21%)	66/327 (20%)

Clinics: 1, Oulu (*n* = 2262); 2, Malmö (*n* = 3713); 3, Gentofte (*n* = 4319); 4, Odense (*n* = 2383); 5, Erlangen (*n* = 728); 6, Amsterdam (*n* = 2915); 7, Leuven (*n* = 3280); 8, London (*n* = 7296); 9, Amersham (*n* = 3068); 10, Almada (*n* = 550); 11, Coimbra (*n* = 1961).
 The number of patients that would have been missed is given as percentage of the total number of patients that were positive to the mix and/or mercapto-benzothiazole. () number of patients tested in each clinic.

Table 2. Number of patients with a positive or negative reaction for mercaptobenzothiazole and the mercapto-mix in the European standard series

	MBT positive	MBT negative	Total
Mercapto-mix pos.	188	73	261
Mercapto-mix neg.	66	–	66
Total	254	73	327

The results are compiled from 11 clinics throughout Europe; total number of patients tested were 32 475, out of which 327 patients were sensitized for at least one of the two Mercapto-compounds.

Practically all clinics would have missed a significant number of positive reactions if both compounds had not been tested. There is no important difference between the clinic (n^4) using the TRUE Test[®] system and the other clinics.

Discussion

Our study shows clearly, in a large group of patients (327 mercapto-compound positive patients), that both the mercapto-mix and MBT are required in the standard series. This confirms other studies which also indicate that a mix in combination with MBT is necessary to detect all your mercapto-sensitive patients (12, 13). Missing on an average of about 20% and 22%, respectively, of sensitized patients is unacceptable.

Based on cross-reactivity studies and a study on the stability of the compounds of the mix it would be sufficient to test with MBT only (8, 14, 15). Several clinical studies suggested that this may be correct and that MBT alone would suffice (9, 16). However, our study clearly demonstrates that a large number of patients would be needed to be able to confirm such a conclusion.

Adding only 0.2% of patients with contact allergy by putting an additional allergen to the standard series does not sound reasonable (17). However, it detects in this case an important extra amount of rubber allergic patients. Of course it would be better to have only one allergen or mix to detect 'all' mercapto-allergic patients. But, there is no alternative so far.

The test concentration of MBT, 1 or 2%, the composition of the mercapto-mix and the concentration of each compound in the mix have been changed several times since the introduction in 1968. Extensive research into the best solution is lacking. It would be interesting to have data comparing the American mercapto-mix with 3 components (not including MBT) and the mix with 4 components (including MBT) used in Europe. The combination of 3 components in combination with MBT as a separate test

material sounds more logical than the present European approach.

For the moment it is advisable to continue with European Standard Series as it is: MBT and the mercapto-mix (4 components) both 2% in petrolatum (18).

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