BRIEF COMMUNICATION

Delayed hypersensitivity to Merthiolate preservative

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In the course of routine allergy investigation, 10 patients were found to have delayed hypersensitivity reactions due to the Merthiolate preservative in the testing solutions. Three patients had had previous contact dermatitis from Merthiolate. Five patients may have been sensitized through either direct contact or parenteral injections, and the mode of sensitization in at least 2 patients was unknown. Delayed local reactions following injection therapy occurred in 2 patients. In view of the availability of phenol, which rarely, if ever, sensitizes, there seems little reason to continue to use Merthiolate as a preservative in allergy extracts.

Delayed hypersensitivity reactions due to Merthiolate have been well recognized.[1-3] This problem may be of practical importance to the clinical allergist because of the frequent incorporation of Merthiolate as a preservative in extracts and diluent. Within a 6 month period in an active allergy clinic, 10 patients who had this cellular-type hypersensitivity to Merthiolate were found. The etiology and possible deleterious effects of Merthiolate sensitivity were pertinent questions resulting from these observations.

CLINICAL DATA

All patients were referred to the Allergy Clinic at Brooke General Hospital for investigation of possible atopic symptoms. For many years it has been standard procedure in this clinic to use allergen extracts and diluent containing Merthiolate as a preservative.* Each patient was tested intradermally with a variety of appropriate allergens.

The diagnosis of Merthiolate sensitivity was established by the occurrence of typical delayed local reactions reaching their peak in 24 to 48 hours at all skin-test sites, including the diluent control. A typical example is noted in Fig. 1. Tests with extracts and diluent containing phenol preservative failed to elicit delayed reactions in any patient.

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*Thimerosal 1:10,000; Hollister-Stier Laboratories, Spokane, Wash.

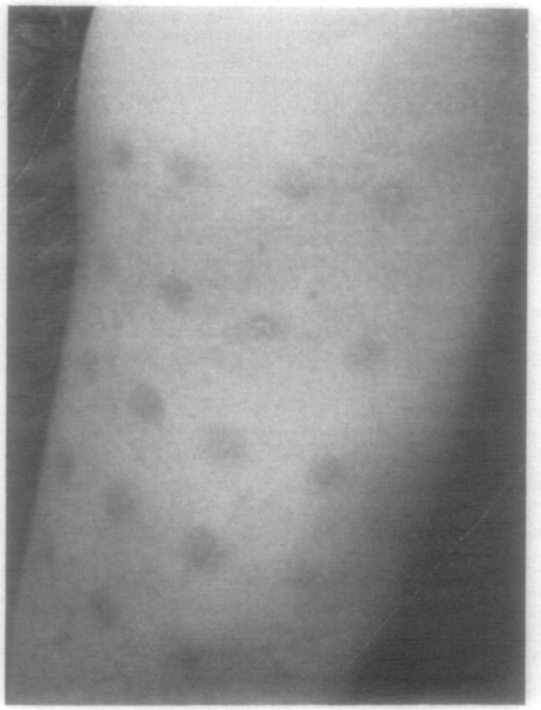


Fig. 1

Delayed hypersensitivity reactions due to Merthiolate preservative. All skin-test sites are reactive (48 hours).

The pertinent clinical data relating to Merthiolate sensitivity are summarized in Table I. There were 8 women and 2 men, ranging in age from 20 to 51 years. Five patients had classical atopic allergies, 2 patients were sensitive to stinging insects, and specific allergy could not be documented in the remaining 3 patients. Six patients had previously used topical Merthiolate. Three of these patients had had a typical contact dermatitis following topical application of Merthiolate. The information regarding these contact reactions was not elicited from any of these patients during their initial interrogation prior to testing.

Five patients had previously received hyposensitization therapy. One patient had received extracts containing Merthiolate, one patient received extracts containing phenol, and the type of preservative used in the extracts given to the other 3 patients was unknown. Two of these 5 patients had experienced delayed local reactions following hyposensitization injections.

DISCUSSION

Merthiolate is sodium ethylmercurithiosalicylate. Previous studies[1, 4] have shown that either the mercurial component or the thiosalicylate component may be the active antigen responsible for eliciting the delayed hypersensitivity reaction. Sensitivity to the thiosalicylate portion has been reported more frequently, and in these instances there is no cross-reaction with other mercurial compounds.

Table I. *Summary of clinical data relating to previous exposure in 10 patients who manifested delayed reactions to Merthiolate*

Patient	*Age (years)*	*Sex*	*Atopy*	*Previous topical application*	*Contact dermatitis*	*Previous hyposensitization therapy*	*Merthiolate-containing extracts*	*Delayed local reactions following hyposensitization*
E. B.	46	F	Yes	Yes		Yes	Uncertain	Yes
M. L.	42	F		Yes	Yes			
J. G.	34	F	Yes (insect)	Yes	Yes	Yes	Yes	Yes
M. S.	51	F				Yes	Uncertain	
D. J.	20	F	Yes			Yes	Uncertain	
L. O.	36	F						
R. B.	26	F	Yes					
R. C.	23	M	Yes	Yes				
S. M.	22	F	Yes (insect)	Yes				
J. B.	39	M	Yes	Yes	Yes	Yes		

It is interesting to speculate regarding the mode of sensitization to Merthiolate. Epstein[2] reported 4 patients with dermatitis of varying causes who were found sensitive to Merthiolate in the course of intradermal tests with such contact allergens as metals and neomycin. Tests with control diluent containing Merthiolate were positive. Apparently there was no relationship between the Merthiolate sensitivity and the etiology of the dermatitis, and in only 1 of 4 patients was there a known history of a previous contact dermatitis from Merthiolate. Thus, the mode of sensitization for these patients was not clear.

Of our patients, 3 had had contact dermatitis following application of Merthiolate many years previously. This occurred prior to the initiation of any allergy injection therapy. Three other patients had used topical Merthiolate in the past without difficulty. One of these 3 did receive injection therapy, but the type of preservative in the solution is unknown. The remaining 4 patients in this study had no recollection of the use of Merthiolate, but it certainly is possible that it had been applied sometime in childhood. Two of these 4 patients had had hyposensitization therapy, but no information regarding the preservative in the solutions was available. Thus, of our 7 patients without a history of contact dermatitis, 3 may have been sensitized through topical application of Merthiolate. Perhaps 2 patients were sensitized by injection of solutions containing Merthiolate, but this is certainly not clear. The mode of sensitization of the remaining 2 patients is unknown. However, it should be noted that some vaccines, such as tetanus, typhus and influenza, and hyperimmune gamma globulin may contain Merthiolate preservative. Patients in this study could have been sensitized in this manner, but specific data are lacking. In order to further elucidate the possible sensitizing role of parenteral injections of solutions containing Merthiolate, 50 patients who had been receiving hyposensitization therapy with Merthiolate-containing extracts for more than 6 months were tested. No positive delayed reactions to the diluent containing Merthiolate preservative were found in any of these 50 patients.

A number of practical considerations arise as a result of Merthiolate sen-

sitivity. Ordinarily there should be no diagnostic problem, as all skin-test sites and the control diluent will react. Immediate reactions to the testing allergen may still occur, and there is no evidence to suggest that this reaction is impaired. Likewise, the occurrence of an immediate reaction does not inhibit the subsequent delayed reaction.

Two of our patients had delayed local reactions following each therapeutic hyposensitization injection, regardless of dosage. It certainly is most reasonable to assume that Merthiolate accounted for these reactions. No systemic effects were noted. Finally, patients whose sensitization was either initiated or perhaps aggravated by Merthiolate injections are certainly prone to contact dermatitis if Merthiolate should be topically applied.

Because of its bactericidal properties, Merthiolate has been used in a concentration of 1:10,000 as a preservative in allergy extracts and diluent. Phenol (0.4 per cent) is probably more widely used as a preservative. It certainly is as effective a bactericidal agent as Merthiolate, and sensitization to phenol has not been reported.

There has been a suggestion that the phenol preservative may reduce the potency of some aqueous allergen extracts which are not affected by Merthiolate.[5] Objective evidence is still lacking. Until such evidence is documented, in view of the occasional occurrence of sensitivity to Merthiolate and the availability of another suitable preservative, there seems little justification in the continued use of Merthiolate in allergy testing and treatment materials.

REFERENCES

1. Ellis, F. A., and Robinson, H. M., Jr.: Cutaneous sensitivity to Merthiolate and other mercurial compounds, Arch. Dermat. & Syph. **46**: 425, 1942.
2. Epstein, S.: Sensitivity to Merthiolate: A cause of false delayed intradermal reactions. Clinical and histological investigations, J. ALLERGY **34**: 225, 1963.
3. Fisher, A. A.: Contact Dermatitis, Philadelphia, 1967, Lea & Febiger, Publishers.
4. Gaul, E. L.: Sensitizing component in thiosalicylic acid, J. Invest. Dermat. **31**: 91, 1958.
5. Stier, R. A.: Personal communication.