

DERMATITIS FOLLOWING THE USE OF PYRIBENZAMINE AND ANTISTINE*

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DESPITE the efficacy of antihistamine drugs in controlling many manifestations of allergy, these drugs may themselves act occasionally as the causative agents of allergic reactions. Several authors^{1, 2, 3} have reported the occurrence of allergic dermatitis following ingestion of Pyribenzamine. Epstein⁴ reported a similar eruption after oral use of Trimeton, which was made worse by an intravenous injection of Benadryl. Strauss⁵ described a case of dermatitis due to local use of Pyribenzamine, and Sulzberger, Baer, and Levin⁶ found 2 of 90 persons tested with Pyribenzamine cream reacted with contact dermatitis. The following is a report of three cases of allergic dermatitis following the use of antihistamine drugs, and the variations in specificity of the sensitization as shown by patch tests.

CASE REPORTS

CASE 1.—M. R., a 46-year-old housewife, was seen Sept. 13, 1948, complaining of dermatitis of the eyelids of 6 weeks' duration. There was a family history of asthma in her maternal grandmother and one niece. The patient had urticaria in childhood and vernal catarrh starting at the age of 38 years but gradually decreasing in severity until she had been practically free from symptoms for two years.

In July, 1948, she noted itching of the eyelids after using Pomatex hair dressing. A physician prescribed Pyribenzamine ointment for local use and Pomatex was discontinued. The itching of the lids stopped but after 5 or 6 days returned in more severe form, with redness and swelling. On one occasion she discontinued the application of the ointment for several days and the lids improved, but failing to recognize the relationship, she resumed its use and gradually became worse. Simultaneous use of Pyribenzamine pills by mouth lessened the itching of the lids but did not affect the appearance of the lesion.

Examination showed the lids to be red and moderately swollen. The conjunctiva were only slightly red. The skin elsewhere was normal. A patch test to Pomatex was applied; a boric compress locally and Pyribenzamine 50 mg. 3 times a day by mouth were prescribed. Two days later she returned with the dermatitis of the lids much worse and stated that because of itching she had continued to apply Pyribenzamine ointment. The patch test with Pomatex showed no reaction. The use of the ointment was stopped but Pyribenzamine by mouth was continued. Within 2 days the lids were normal and remained so until the patient was last seen one month later.

Patch tests with Pyribenzamine powder† gave a 4 plus reaction. There was no reaction to Neo-Antergan, Antistine, Neohetramine, Trimeton, or Benadryl. Pyribenzamine cream and ointment gave 2 plus reactions.

The original cause of itching of the eyelids was not established but the dermatitis observed was undoubtedly due to Pyribenzamine ointment.

CASE 2.—Mrs. F. B., a 56-year-old teacher was seen Oct. 21, 1948, complaining of intermittent dermatitis for 5 months. There was no family history of allergy, but the patient had a severe urticarial eruption following the use of a sulfonamide drug in 1943.

In May, 1948, she first noted a dermatitis of the neck which failed to respond to treatment with ultraviolet light and was followed by similar involvement of the eyelids. She

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†Supplied by Ciba Pharmaceutical Products, Inc., Summit, N. J.

spent the summer in the country where she wore cottons during the week, rayons and silks on Sunday, on which day she regularly applied Revlon nail polish and Adheron lacquer to her nails. The skin eruption regularly became worse on Sundays and Mondays and subsided during the remainder of the week.

A physician advised discarding the nail polish and lacquer and prescribed Pyribenzamine ointment. During the following 2 weeks the eruption disappeared, then suddenly recurred. Subsequently she noted a marked exacerbation of the dermatitis of the neck and eyelids on three occasions after the use of Lustre Cream shampoo.

On examination there was a marked redness, thickening and scaling of the skin of the eyelids and cheeks, extending in a less marked form over the neck to the clavicles. The remainder of the skin was normal.

Patch tests with her nail polish, Adheron lacquer, and Lustre Cream shampoo (5% solution) gave 3 plus reactions; her other cosmetics showed no reaction.

She was advised to discontinue all cosmetics and shampoos but was permitted to continue the use of Pyribenzamine ointment previously prescribed. During the following week the rash on the face and neck became progressively worse until she was admitted to the hospital. The Pyribenzamine ointment was then discontinued and aluminum acetate wet dressings were applied. Within 3 days the skin eruption disappeared and except for a brief recurrence after she had applied plastic varnish to some furniture, she remained well until last seen 2 months later.

Patch tests with antihistamine drugs showed a 3 plus reaction to Pyribenzamine, 2 plus reactions to Neo-Antergan and Thenylene; no reactions to Antistine, Diatrin, Neohetramine, Trimeton, Benadryl, or Theophorin. Pyribenzamine ointment and cream gave positive reactions, somewhat less marked than those to the pure powdered drug.

In this case, the contact dermatitis was originally caused by sensitization to nail polish, Adheron lacquer and Lustre Cream shampoo, but was aggravated by Pyribenzamine ointment after contact with the original agents was discontinued.

CASE 3.—C. H., a 54-year-old graduate nurse, was first seen Nov. 30, 1948, complaining of swelling and redness of the eyelids. There was a family history of asthma in her maternal grandmother, and the patient had eczema of the face and hands at the age of 9 years. The past history was otherwise irrelevant.

She noted irritation of the eyes Oct. 13, 1948, after using paradichlorbenzene as a moth preventive. Antistine eye drops were prescribed and the inflammation subsided in 4 days. She remained well for one month, then redness of the eyes recurred. She again used the Antistine eye drops for one day, then an ophthalmologist advised cold compresses and Pyribenzamine by mouth. Five days later the use of Antistine eye drops was resumed and within 24 hours there was marked redness and swelling of the eyelids.

When seen the next day there was marked edema of the eyelids with an area of red, oozing, vesicular dermatitis covering the lids and upper parts of the cheeks. The skin of the back and chest showed a diffuse maculopapular rash most marked below the axillae.

The Antistine eye drops and the Pyribenzamine were discontinued and boric compresses applied to the eyes and cheeks. Within 3 days the condition of the face was markedly improved and the rash on the body was fading.

Patch tests with her rouge showed a 2 plus reaction, the rest of her cosmetics showed no reactions, nor did paradichlorbenzene. Patch tests with various antihistamine drugs showed 3 plus reactions to Pyribenzamine, Antistine, Neo-Antergan, and Diatrin; 2 plus reactions to Thenylene, Neohetramine, Trimeton, and Benadryl. There was no reaction to Theophorin.

With all medications withheld, the skin cleared uneventfully, although, when seen in March, 1949, the patient reported that she also had a local reaction to Pontocaine ointment used for pruritus ani. At that time the skin of the eyelids was slightly thickened and itchy but not inflamed.

This patient showed evidence of sensitivity to a wide variety of antihistamine drugs. The contact dermatitis of the eyelids which was apparently initiated by the nonspecific irritant effect of paradichlorbenzene and allergy to rouge was greatly aggravated by Antistine eye drops and the dermatitis of the body was probably due to oral use of Pyribenzamine.

DISCUSSION

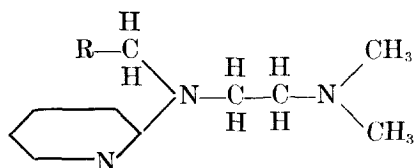
Exacerbations of contact dermatitis of the eyelids, face, and neck were shown by patch tests and clinical observations to be due to Pyribenzamine ointment in 2 cases and to Antistine eye drops in one case. In the last patient, who showed reactions to many antihistamine drugs, there was also a maculopapular rash of the trunk apparently due to oral use of Pyribenzamine. The possibility that oral use of Pyribenzamine contributed to the eruption on the face of this patient was not evaluated since Antistine eye drops and Pyribenzamine tablets were discontinued at the same time.

In the case of the first patient, the skin rash disappeared after stopping local use of Pyribenzamine ointment while oral use of Pyribenzamine tablets, 50 mg. 3 times daily, was continued. This is contrary to the frequent observation that sites of previous contact dermatitis caused by local use of drugs, such as the sulfonamides, flare up when the same drug is given by mouth. Such reactions presumably depend on the degree of sensitivity and the concentrations of drug in the blood stream. Since the total daily dose of Pyribenzamine was only 150 mg., as compared to a daily dose of 4 to 6 grams for the sulfonamides, the lack of such a reaction is understandable.

No separate tests were made with ointment base but simultaneous tests with pure powdered Pyribenzamine, Pyribenzamine ointment, and Pyribenzamine cream in each case showed the reaction to be greatest to the pure powdered drug, so there was no reason to suspect the base as a causative agent. Control patch tests with powdered Pyribenzamine and Antistine eye drops on 3 normal persons showed no reaction.

All 3 patients gave past histories of allergic manifestations, 2 showing reactions to patch tests with other types of agents, and in all instances the drugs were used for several days before evidence of sensitization was apparent.

The 3 cases illustrate strikingly the variations in specificity of such sensitivities. One patient (Case 1) reacted strongly to Pyribenzamine but showed no reaction to 5 other drugs of the group. The second patient (Case 2) showed reactions to Pyribenzamine, Neo-Antergan and Thenylene, all of which have the common structure,



but not to 6 other drugs of the group which do not have this structure. The third patient (Case 3) reacted to 8 antihistamine drugs showing considerable variations in chemical structure, but not to Thephorin, the formula of which differs markedly from others of the group.

TABLE I

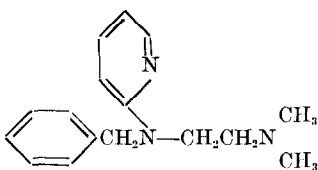
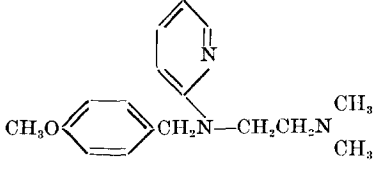
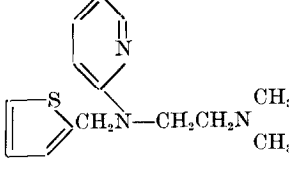
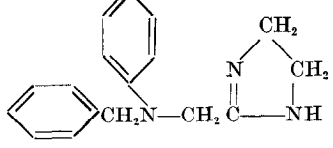
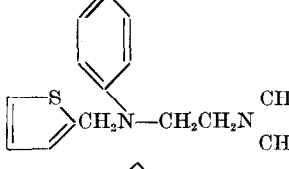
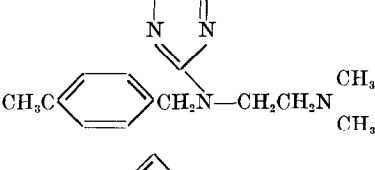
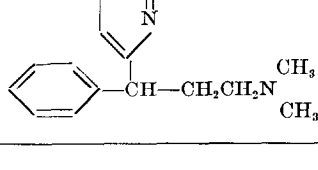
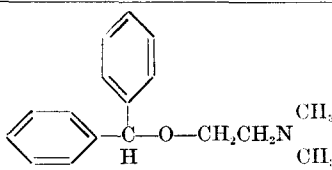
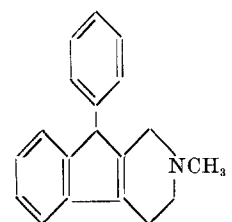
DRUG	FORMULA	REACTIONS		
		CASE 1	CASE 2	CASE 3
Pyribenzamine		+++	+++	+++
Neo-Antergan		0	++	+++
Thenylene		-	++	++
Antistine		0	0	+++
Diatrin		-	0	+++
Neohetramine		0	0	++
Trimeton		0	0	++

TABLE I—CONT'D

DRUG	FORMULA	REACTIONS		
		CASE 1	CASE 2	CASE 3
Benadryl		0	0	++
Thephorin		-	0	0

SUMMARY

1. Exacerbations of contact dermatitis of the face and neck were shown by clinical observations and patch tests to be due in 2 cases to Pyribenzamine ointment and in one to Antistine eye drops. The latter patient also had dermatitis medicamentosa apparently due to Pyribenzamine taken by mouth.

2. All 3 patients had past histories of allergic disease and 2 had contact dermatitis due to other agents.

3. In each case, the drugs were used for several days before evidence of sensitization was apparent.

4. One patient reacted on patch tests to Pyribenzamine but not to other drugs of the group; the second reacted to Pyribenzamine, Thenylene, and Neo-Antergan but not to 6 other antihistamine drugs; the third reacted to 8 antihistamine drugs but not to Thephorin which differs markedly from the others in chemical structure.

REFERENCES

1. Epstein, E.: Dermatitis Occurring During Therapy With Tripeleminamine Hydrochloride (Pyribenzamine Hydrochloride), *J. A. M. A.* **134**: 782, 1947.
2. Harris, M. C., and Shure, N.: Eczematoid Dermatitis Following Ingestion of "Pyribenzamine Hydrochloride" N.N.R. Tablets, *J. ALLERGY* **18**: 408, 1947.
3. Ratner, H., and Graffin, J.: Dermatitis Due to Pyribenzamine, *Am. Practitioner* **2**: 754, 1948.
4. Epstein, E.: Dermatitis Due to Antihistamine Agents, *J. Invest. Dermat.* **12**: 151, 1949.
5. Strauss, M. J.: Eczematous Contact-Type Allergy to Pyribenzamine, *J. Invest. Dermat.* **11**: 155, 1948.
6. Sulzberger, M., Baer, R., and Levin, H. B.: Local Therapy With Pyribenzamine Hydrochloride, *J. Invest. Dermat.* **10**: 41, 1948.