

ALLERGIC STOMATITIS FROM MEDICATED THROAT LOZENGE

Report of a Case

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THE buccal mucosa is an uncommon site of allergic sensitization. In the reported cases of allergic stomatitis of the contact type, also known as stomatitis venenata, the causative agents have included chewing gum, tooth pastes, and many kinds of lozenges, including the medicated throat discs or troches. In recent years, troches containing various antibiotics, especially penicillin, have been frequent offenders. As a result, penicillin troches seldom are used at present because of their marked sensitizing potentialities. Troches containing other antibiotics, usually either neomycin or bacitracin, are poor sensitizers and rarely induce stomatitis. Most of the reported reactions have been mild and subacute, or chronic in character. Recently we encountered an instance of an acute allergic stomatitis from a commonly used troche which, so far as we can determine, rarely induces such an allergic reaction. This forms the basis of the present report.

CASE HISTORY

The patient is a woman, 35 years of age, who has been under treatment since 1954 because of seasonal and perennial allergic rhinitis and asthma, and generalized atopic dermatitis. She showed marked improvement from allergy treatment, despite her extreme sensitivity to the allergenic extracts used in treatment, which made it necessary to use high dilutions of the extracts so that they could be administered without aggravating the allergic dermatitis. Even the small amount of phenol (0.5 per cent), employed as a preservative in the diluent, seemed to induce a reaction. The patient also seemed intolerant of such drugs as amylal and iodides. Oral cortisone on two occasions induced anuria.

At irregular intervals, during a period of several years, the patient had mild to moderate attacks of pharyngitis followed or associated with either laryngitis or bronchitis or both. In the initial stages when the pharyngitis was mild she would take throat lozenges. If it became more severe, she would then take Achromycin orally. Several kinds of throat lozenges were taken by the patient, all at the suggestion of her pharmacist, the ones used most frequently were Lozilles.* At other times she took Candettes,† as well as varied proprietary candy lozenges (Smith Bros. cough drops, Pine Bros. honey lozenge,‡ etc.) without difficulty.

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In late April, 1961, she again developed pharyngitis. Because her druggist did not happen to have any of her usual lozenges in stock, he suggested that she try Thantis lozenges.* She took one upon arising and one 6 hours later without any noticeable untoward after-effects. The pharyngitis improved temporarily. A week later the pharyngitis recurred and she again took a Thantis lozenge. She took only a half tablet and kept it on the inner left side of the mouth. Instead of being improved, her throat seemed more sore. She then took a whole lozenge and again put it in the left side of the oral cavity. Within about 15 minutes, the whole inner side of the mouth felt raw; and when she looked at it in the mirror, she noted minute "blisters" on the gums, on the inside of the oral cavity of both sides of the mouth, and on the inner side of the tongue. Shortly thereafter, she felt she was choking and had difficulty in swallowing. She took a tablet of Pyribenzamine, which seemed to ease the choking, but the throat still felt quite raw.

When she consulted one of us (L. T.) the next day, her throat still was quite sore. On inspection, a whitish exudate was seen on the buccal mucosa in the molar region of both sides of the mouth. The mucosa visible in back of the exudate was inflamed on both sides but more so on the left side. The left submaxillary glands were rather tender and swollen. She was given an alkaline mouth wash and reported gradual improvement with return to normal after 4 days. When she was seen a week after the initial visit for the pharyngitis, the throat was normal in appearance. There was no evidence of exudate or of inflammation, and the tenderness in the left submaxillary gland had disappeared. A smear taken from the exudate and stained with Wright's stain showed eosinophils, roughly estimated at 8 per cent.

Upon further questioning, the patient stated that she had never used Thantis previously. She recalled having had merthiolate applied to her abdomen preoperatively in 1956, and applications of mercurochrome to her skin at various times during her childhood without any untoward after-effects.

CLINICAL STUDIES

It seemed probable from the history and examination that the condition the patient presented was that of allergic stomatitis of the contact type, probably due to sensitivity to one of the ingredients of the Thantis lozenge. In order to investigate this further we obtained, from the manufacturer, samples of the various ingredients of the lozenge for use in a patch-test study. In our request for these samples, we asked the manufacturer if anyone had reported any similar reactions to them. In the reply we were told that "Thantis Lozenges have been on the market since 1930 and millions of lozenges have been consumed up to the present time. Infrequently, reports have reached us of mouth reactions and usually these have been traced to a personal idiosyncrasy."

They listed the following substances as ingredients of the lozenge: mero-dicein, saligenin, oil of peppermint, calcium carbonate, menthol, cane sugar, corn sugar, stearic acid, and white mineral oil.

All of the above materials then were used in the concentration present in the lozenge for the patch-test study. These were applied to the skin of the outer surfaces of both arms and flexor surfaces of both forearms and covered with the patch. A patch test also was done with a small amount of powdered scrapings from a Thantis lozenge which the patient still had left in the original vial from which she had taken the first lozenges. Because of her sensitivity to adhesive, Scotch Tape was used to cover the materials instead of the usual ad-

*These are manufactured by Hynson, Westcott, & Dunning (Baltimore, Md.) to whom we are indebted for supplying the ingredients of the lozenge employed in the patch-test study.

hesive patch. The patches were removed at the end of 48 hours and the sites inspected for reaction at that time and again at intervals up to 5 days. Completely negative reactions were obtained to stearic acid, oil of peppermint, cane sugar, mineral oil, menthol, corn sugar, calcium carbonate, and to the solution of merodicein. By contrast, strongly positive reactions were observed at the end of 48 hours at the sites of the Thantis lozenge (Fig. 1) and of the solution of saligenin (1 gram in 17 c.c. water). The reaction in both instances consisted of a large erythematous swelling about 2 cm. in diameter with small vesicles within the lesion. These reactions gradually subsided and finally disappeared at the end of another week.



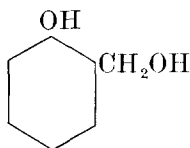
Fig. 1.

In order to find out whether they might be irritating to the normal skin, patch tests were done on control patients with solutions of merodicein and of saligenin, as well as with powdered Thantis lozenge and mineral oil. None of the 20 controls reacted to either mineral oil or to saligenin and none of 11 controls reacted to the powdered Thantis lozenge. One of the 20 controls tested with merodicein showed a slight positive reaction, the cause of which could not be determined.

As a result of these patch-test studies, it seemed rather definitely established that the ingredient of the Thantis lozenge responsible for the allergic reaction in our patient was saligenin.

COMMENT

Our first inclination upon finding out the ingredients of the Thantis lozenge was to attribute the sensitization to the merodicein because it was a mercurial, and mercurial compounds are notoriously potent sensitizers. We were surprised therefore at the results of the patch tests which incriminated saligenin as the offending agent. But this was not too surprising since saligenin is a member of the "caine" family of anesthetic agents which likewise are fairly potent sensitizers. Saligenin, also known as salicaine, is prepared from phenol and formaldehyde which oxidizes in the body to form salicyl aldehyde and salicylic acid.



Because of its rather low toxicity, it formerly was used in 2 to 4 per cent solutions for local anesthetic purposes. According to Hirschfelder and Bieter,¹ it may be satisfactory for infiltration anesthesia of not too long duration but is useless for nerve block and for spinal anesthesia. On the whole it is much inferior to similar agents (such as cocaine, eucaine, procaine, etc.) as a local anesthetic. Weak solutions of saligenin have no effects upon mucous membranes—however, marked dulling of sensation follows the application of a freshly prepared 12 per cent solution to the oral and nasal mucosa.

Allergy of the contact type due to sensitization to saligenin is quite uncommon, judging at least from review of the literature. Brunsting and Brunsting² in 1937 reported a case of contact allergic dermatitis of the buttocks due to sensitivity to saligenin which had been incorporated into the solution of iodo-bismitol with which the patient was being treated for neurosyphilis. Patch tests were positive to saligenin and negative to all other ingredients—furthermore, following the elimination of this agent from the stock solution, the latter was given to the patient subsequently without any reaction. Except for this case report, we have been unable to find any other reports of an allergic reaction to saligenin, either affecting the skin or the buccal mucosa. It is not unlikely that such reactions occur and have not been reported, but the incidence on the whole must be extremely low. In view of its extreme rarity, the question of treatment seldom arises. The only form of therapy required is strict avoidance of any lozenges containing saligenin. Specific desensitization is neither required nor needed. Treatment of the reaction itself consists in the use of mild alkaline mouth washes and the administration of antihistamines orally, especially in the early stages.

SUMMARY

A rare instance of acute allergic stomatitis of the contact type (stomatitis venenata) provoked by a medicated throat lozenge (Thantis) is reported. It

proved, by patch tests with all of the ingredients of the lozenge, to be due to a contact allergy to saligenin (salicaine), a local anesthetic agent.

REFERENCES

1. Hirschfelder, A. D., and Bieter, R. N.: *Physiol. Rev.* **12**: 190, 1932.
2. Brunsting, H. A., and Brunsting, L. A.: *Dermatitis of the Buttocks Due to Saligenin*, *Arch. Dermat. & Syph.* **36**: 1187, 1937.