STUDIES IN MUCOUS MEMBRANE SENSITIZATION

Part III. The Effects of Toothpowder Containing Penicillin*

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The technics for detecting potential and actual eczematous hypersensitivity of the buccal mucosa have been reported before (1, 2, 3). Interest in this work is continued by the increasing use of penicillin and other antibiotics in the mouth for oral surgery, oral pathology, dental caries, etc. Our primary concern in this study is the relationship of repeated and long continued use of penicillin to sensitization of the buccal mucosa.

McClure and Hewitt (4) added penicillin to the drinking water supply and to a dental caries-producing diet of rats, and reported a great reduction in the development of caries. Zander and Bibby (5) found that penicillin prevented the production of acid in saliva *in vitro* and *in vivo*. He also reported that brushing the teeth of hamsters twice daily with a dentifrice containing 1000 units of penicillin per gram virtually prevented dental caries. Hill (6) has reported a study in which he used a penicillin dentifrice on a small group of students and obtained a significant decrease in lactobacillus count.

EXPERIMENT I

For the present study we used a tooth powder similar to that used by Zander, consisting of calcium phosphate, a wetting agent, flavor and 500 units of penicillin G per gram. The powder was packaged in the ordinary metal containers commonly found on the market. The identical container and tooth powder (without penicillin) was used as the control. Assays showed the penicillin to be stable in the mixture longer than the 10 week testing period.

In most patients, the "cotton pledget," one hour contact on the mucous membrane of the upper lip method was used. One side of the mouth was tested with the control, and the other side tested simultaneously with the penicillin containing toothpowder. A contact period of one hour was regularly employed, although in some cases this was done for as long as twenty-four hours. In a few instances the pledgets were replaced with fresh ones at variable intervals after the first hour in order to attempt to emphasize any latent reactions. The mouth was washed out well with water before and after each test to insure better contact, better visualization, etc. If during the first hour of contact, the patient failed to retain the pledget properly and immediate replacement was not possible, the results were not included in this series. In some instances small cups fixed to the teeth were used for testing aids. Results were checked immediately after re-

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moval at the end of the first hour, and at intervals in the next twenty-four hours. 107 patients were tested in our preliminary phase.

RESULTS

Of the 107 patients so tested, 42 had never had prior contact with penicillin so far as could be determined. 41 of the patients showed no reactions to either the control or the penicillin type toothpowder. The remaining patient showed an indeterminate reaction to both powders; prolonging the test period did not increase reactions.

Of the remaining 65 patients in our preliminary series who were known to have had contact with penicillin in some manner, 6 had been shown to have had penicillin reactions in the past. We did not observe these reactions. None showed reactions of the buccal mucosa at the time of testing. The remaining 59 patients of this group showed no reactions except one patient who had been suspected of being penicillin sensitive in the past. Only indeterminate reactions to the

TABLE 1

Reactions in patients with a history of reactions to penicillin

CASE NO.	CONTROL	PCN. TOOTH POWDER	COURSE
1	0	3+ 1 hr.	flare in 36 hours
2	0	2+ 1 hr.	
3	0	0 1 hr.	
4	0	0 1 hr.	
5	0	0 1 hr.	severe stomatitis at 72 hrs.
6	0	0 1 hr.	1+ 5 hrs., 3+ 24 hrs.

powder and control were found. Five other patients gave a history that indicated possible penicillin sensitivity in the past, but in all five cases, reactions to both powders were negative.

Reactions of the buccal mucosal test varied from simple erythema to erythema-edema and vesiculo-bullous reactions. It was our impression from this preliminary study that persons with known sensitivity to penicillin, especially of the eczematous type, do get reactions from buccal mucosa contact tests to penicillin. As far as we can determine at this time, there is no evidence that such testing has produced sensitization in persons not previously sensitive to penicillin. We do not know the value of such a penicillin mixture for hyposensitization.

EXPERIMENT II

Following these preliminary test studies, we attempted to use the penicillin containing toothpowder in patients who were known to be sensitive to penicillin. As soon as the reaction from penicillin subsided, we made simultaneous patch, scratch, intradermal and buccal mucous membrane tests (with the control and the penicillin toothpowder). These tests were followed immediately with the actual oral use of the toothpowder containing penicillin. The mixture was used

as a dentrifrice at least twice daily. The patch tests were done with the penicillin ointment containing 1000 U/Gm. The intradermal and scratch tests were done with aqueous solutions containing 500 U/.10 cc. solution. Such low concentrations for intradermal testing were used in an attempt to evaluate the initial erythema-edema reaction. The scratch and intradermal tests were read at 15–30 minutes and at 48 hours, and if indicated, again at 72 hours. Patch tests were read at 48 hours and later. Buccal mucous membrane tests were checked at one hour and later as noted. In many instances, simultaneous testing to streptomycin was carried out. As often as possible, the patient began using the penicillin tooth-powder within the first twenty-four hours after the reading of the buccal mucosa test.

RESULTS

We were able to test 18 patients with definite reactions to penicillin. These patients were followed through our Penicillin Reaction Center. Of these 18 patients, 7 exhibited angio-edema-urticarial types of reactions. Of these 7, 5 patients exhibited negative reactions to all the various tests, and used the penicillin tooth-powder for periods of time varying from 1–4 weeks with no visible ill effects. One patient showed negative patch, scratch, and buccal mucous membrane tests, and a 1+ intradermal reaction at 48 hours. He used the powder for 4 weeks without any reactions noted. Urticaria present at the start of the actual use of the toothpowder subsided rapidly. The 7th patient showed marked urticaria, fever, angio-edema, and hydrarthosis. The intradermal, patch, and scratch tests were negative in 48 hours. The buccal mucosa test for the control powder was negative, and remained so throughout his course. The buccal mucosa test to the penicillin powder was 3+ in 1 hour, and later the patient complained of burning sensations in the mouth. In 48 hours there was a fine papulo-vesicular stomatitis involving the cheeks and palate regions with some milder erythema of the tongue. As yet, no usage testing has been done on this patient.

3 of the 18 patients presented maculo-papular types of eruptions. In all three instances all tests were negative. All have employed the dentifrice from 3–4 weeks without any apparent harm.

4 cases showing papulo-vesicular reactions were seen. Two of these showed negative results to all the tests, and have used the penicillin containing tooth-powder from 1–5 weeks with no reactions noted. One patient, when tested in the acute phase, showed a strongly positive test, and no powder was used. However, as soon as his acute stage had subsided, repeated tests on the same sites with the same materials produced all negative results, and the patient used the dentifrice twice daily for 5 weeks with no harm. The fourth case, a senior medical student, showed a very marked papulo-vesicular type of reaction involving the hands, feet, scalp, and scrotum. In addition to this, he showed numerous urticarial and angio-edematous lesions of the body, face and eyelids. These symptoms were accompanied by flaring of a dormant tinea pedis and pruritus ani. The patch tests were negative in 48 hours, scratch test gave a strong immediate reaction, but faded rapidly and was negative in 48 hours. The intradermal test was strongly

positive and was followed by an eczematoid response. The control toothpowder gave no reactions. The penicillin toothpowder gave a strong positive reaction in one hour, and the patient stated that his throat felt somewhat dry. Within 24 hours after the start of the tests, there was a decrease in the urticarial elements as a whole, but local urticaria appeared at the sites of recent injections of procaine penicillin G in oil in the gluteal muscles. These subsided within the following 48 hours. The papulo-vesicular elements gradually subsided within the next week. Penicillin toothpowder as a daily dentifrice b.i.d. was started cautiously within the first 24 hours of observation. To date he has used it 18 days without any complaints.

4 cases were found to present an eczematoid contact type reaction. In these cases, in addition to the tests used before, we made simultaneous patch tests with the penicillin toothpowder moistened to about the same concentration as would be found in the mouth in the usual hour contact period. All of these latter patch tests were negative in 48 hours. All 4 patients showed 2+ to 4+ reactions to the usual 48 hour patch tests with the penicillin ointment. Apparently the toothpowder mixture was not able to elicit reactions. 3 of the 4 patients showed negative reactions to all the other tests, and have used the toothpowder for 2–4 weeks without trouble. The 4th patient, in addition to 4+ reaction to the ointment, had 2+ reactions for his intradermal and scratch tests, but negative buccal mucosa tests. Use of the powder for approximately 8 days to date has not produced any further reactions.

DISCUSSION

Rattner (7) using the identical mixture as a daily dentifrice in three cases of proven penicillin sensitivity for periods of 7–10 days reported no ill effects. Peck (8) has also employed this same product for 8 cases of penicillin sensitive patients with results that closely resemble ours, in that in spite of recent or active reactions upon the skin, use of the toothpowder caused little, if any trouble in these cases. Welsh (9) has also used the same material for four cases of penicillin sensitivity (not tested) for periods of 1–3 weeks without ill effects except slight cheilitis in one case. Zander photographed the few instances of eruptions about the mouth or lips that he noted in his series of school children using this mixture for approximately 15 months to date. We have examined the photographs of 4 reported. These all involved the lips or commissures of the mouth, and were not severe. They resembled perlèche or slightly eczematoid contact dermatitis of the carmine borders of the lips as sometimes seen in lipstick dermatitis. The control group in this series presented an almost similar picture and were of almost the same number. The report included no other skin eruptions, and no tests had been done.

CONCLUSIONS

1. A buccal mucous membrane contact test with a toothpowder containing 500 units of penicillin G per gram, in 107 patients, revealed that patients with

previous known penicillin hypersensitivity do sometimes show definite reactions to such mucosal tests.

2. Such buccal mucosal testing did not appear to sensitize previously non-sensitive individuals.

3. In 18 cases of known and established penicillin hypersensitivity, buccal mucosal contact tests, in conjunction with cutaneous scratch, intradermal and patch tests, indicate that a positive mucous membrane test may develop either in agreement with or in opposition to the simultaneous cutaneous tests, even of the contact type. It is possible that better standardization of the buccal mucosal contact test may serve to increase the number of positive reactions of this type of contact testing.

4. Preliminary studies of small groups of patients indicate that a toothpowder reported to contain 500 units of penicillin per gram used as an ordinary dentifrice twice a day by individuals with known, occasionally still active, penicillin hypersensitivity, produces few local reactions and no known systemic reactions.

5. This study furnishes additional evidence for the greater difficulty of inducing contact stomatitis as opposed to contact dermatitis.

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