

# ANAPHYLACTIC REACTION FROM TOPICAL PENICILLIN

## REPORT OF A CASE

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THE primary purpose of this paper is to report a case of immediate reaction following the antral instillation of penicillin. The literature contains only one other report describing two similar cases of penicillin reactions.<sup>1</sup> Doubtless otolaryngologists have encountered others which remain hitherto unreported. Any inferences arising from the discussion of this case constitute nothing new, but simply a review of some of the more clinically important and related aspects of penicillin sensitivity.

## CASE REPORT

I. K., a 30-year-old white female hospital attendant, was treated at the Cushing Veterans Administration Hospital, Framingham, Mass., in December of 1946 for a right antral sinusitis. About a year later an antrostomy was performed because of a flare-up. On both occasions she was given a series of intramuscular injections of procaine penicillin. On July 30, 1951, an antrostomy was performed on the left side for a draining sinus which followed the extraction of an abscessed tooth. On this occasion she was placed on oral penicillin. On the fifth day of oral penicillin she developed mild tingling of the palms of the hands, soles of the feet, and vulvar region. At this point the patient discontinued the penicillin of her own accord.

On Aug. 8, 1951, she reported to the E.N.T. Section of the Boston Veterans Administration Regional Office for further treatment. On this date the left antrum was irrigated with saline solution with no untoward reaction and the patient was placed on Aureomycin therapy. Several days later, and because of essentially no improvement, 100,000 units of crystalline penicillin G in 2 ml. of distilled water was instilled into the left antrum through the antrostomy opening. Within a matter of seconds she complained of nausea, weakness and faintness, burning and itching of the hands and feet and generalized tingling. She sneezed several times. Wheezing of a mild degree was present. Beginning with the hands, her entire body soon became erythematous and edematous. The conjunctivae were injected and chemotic. The pulse was somewhat weak and rapid at a rate of 160; the blood pressure, 80/60. At no time was she pale and sweaty nor did she lose consciousness. Within several minutes after the onset of the reaction 0.5 ml. of epinephrine hydrochloride 1:1,000 was administered hypodermically and this was followed by 100 mg. of tripeleennamine hydrochloride administered orally. Within an hour all symptoms gradually disappeared and the patient felt quite normal.

The patient's family and past history were devoid of any atopic background. There was no history or evidence of any mycotic disease of the skin. Routine intradermal tests for inhalants, pollens, and molds disclosed a borderline reaction to house dust and *Alternaria*. On Sept. 13, 1951, skin tests were performed with crystalline penicillin G taken from the same batch of penicillin that produced the reaction. The scratch test was quite

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From the Allergy Section of the Regional Office, Veterans Administration.

Presented at the Ninth Annual Meeting of the American Academy of Allergy, Boston, Mass., Feb. 28, 1953.

Received for publication Feb. 12, 1953.

positive in a dilution of 10,000 units per ml. A wheal with pseudopods and measuring about 3 cm. in diameter and with a marked flare was obtained by intracutaneous testing with 0.02 ml. of solution containing 1,000 units per ml. A drop of solution, containing 50,000 units per ml., and applied directly to the skin, had to be wiped away because of immediate itching and erythema. The delayed reaction, read in forty-eight hours, was also positive, the papule measuring 1.4 cm. in diameter. The trichophyton test was not done. An attempt to demonstrate circulating antibodies on two normal recipients proved unsuccessful. Fourteen months later this patient was retested in connection with comparative studies on penicillin G and O and found to be negative to the immediate and delayed reactions of both penicillins. Inhalation aerosol with both penicillins failed to produce bronchospasm or any diminution in vital capacity.

#### DISCUSSION

The pattern of this case closely parallels the two cases reported by Everett.<sup>1</sup> In both his cases the reaction following antral instillation of penicillin was virtually immediate. The reaction in the first case, a nonatopic, was apparently the first indication of penicillin sensitivity. The reaction in the second case, an atopic asthmatic, had been preceded by mild itching associated with both oral and aerosol penicillin. Again, in both cases, there had been previous antral instillations with penicillin. Unfortunately, it was not possible definitely to ascertain from either the patient or the hospital records whether or not penicillin had been instilled into the sinus at any time prior to the reaction. Such information might well be of primary interest to the otolaryngologist. In all three cases the reactions were preceded by recent administration of penicillin in one form or another, thus bearing out the observation of Keefer<sup>2</sup> that the closer the intervals between administration the greater the likelihood of reaction. All three cases had repeated courses of penicillin. Keefer<sup>2</sup> and Long<sup>3</sup> have pointed out that such a situation serves to increase the potentiality of sensitization.

Everett's<sup>1</sup> first case was associated with marked bronchospasm, severe circulatory depression, and no dermal reaction (urticaria). Higgins and Rothchild,<sup>4</sup> in reporting a case of fatal anaphylactic shock from procaine penicillin which more closely resembles animal anaphylaxis, also reviewed previously reported anaphylactic reactions to penicillin. They point out that Everett's<sup>1</sup> second case, associated with bronchospasm and dermal reaction but no shock-like symptoms, did not constitute a true anaphylactic reaction. Depending on one's definition of anaphylactic reaction in the human being, one might seriously question as to whether or not the reaction reported could correctly be termed as anaphylactic. Burleson,<sup>5</sup> in describing his case of wheezing, dermal reaction, and shock following intramuscular procaine penicillin, used the term "anaphylactoid." This case was also preceded by several courses of penicillin in the past followed subsequently with oral penicillin, the latter producing the first indication of sensitivity, namely, slight itching. Irwin, Graham, Jacobson, and Burrage<sup>6</sup> referred to their case as one "of a shock-like type of reaction" associated with an "atopic type of penicillin sensitivity." For purposes of more accurate description it would appear more suitable to label this reaction as a severe immediate allergic reaction associated with some de-

gree of shocklike symptoms. It is conceivable, however, that had not epinephrine been administered so promptly, more imposing shocklike symptoms might have supervened.

It is not uncommon, as seen in this case, for both the immediate and delayed skin tests to become negative at some future time after the reaction. Penicillin, with its amino acid-like structure, is regarded as a poor antigen. McClosky<sup>7</sup> suggests that its low molecular weight may account for its irregular ability to act antigenically. It is commonly believed that haptene formation plays the larger role in penicillin reactions particularly in the non-atopic individual. It is noteworthy that, in the case of Irwin and associates,<sup>6</sup> atopic in character, with marked skin reactions and the presence of circulating antibodies, both the immediate and delayed tests also turned negative some months later.<sup>8</sup> Peek and his co-workers<sup>9</sup> have demonstrated the unreliability of the skin test and that not infrequently reactions develop in individuals negative to both the immediate and delayed skin test. Everett<sup>1</sup> made no reference to skin tests but, again, it is noteworthy that his first patient experienced a profound degree of shock from intramuscular penicillin administered inadvertently by another physician several months after the first reaction.

Considering the widespread use of penicillin these past ten years, the literature contains very few reports of the so-called "anaphylactic" and more immediate types of reactions. A recent editorial<sup>10</sup> in *THE JOURNAL OF ALLERGY* points out that there have been many more fatal cases and alarming reactions which have not been reported. Keefer<sup>2</sup> states that the greatest incidence of sensitization arises from topical administration and the least from the oral route. As more people receive an increasing number of penicillin courses and subsequently take oral penicillin, oral sensitization may assume greater importance. The symptoms are usually mild in character such as slight tingling or itching of the hands and feet and are frequently overlooked by the patient or disregarded by the physician. Doubtless many alarming reactions and even some deaths have ensued during the course of treatment with agents capable of producing anaphylactic reactions at a time when the physician failed to pay attention to that slight itching of the palms or other premonitory symptoms. The history of mild sensitivity associated with oral ingestion of penicillin was not obtained in this patient chiefly because of the patient's lack of understanding of the term "sensitivity." One author of a recent paper on penicillin reactions expostulated in this regard that the patient should be questioned in a language that could be clearly understood.

#### SUMMARY

1. A case of severe immediate allergic reaction following the antral instillation of penicillin has been presented.
2. Two other similar cases noted in the literature have been reviewed.
3. The use of the term "anaphylactic" and some of the related aspects of penicillin sensitivity have been discussed.
4. More careful attention should be paid to the patient's pre-existing sensitivities in the use of penicillin.

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