

Editorial

FATAL ALLERGIC REACTIONS TO PENICILLIN

Waldbott, in 1948, reported a case of sudden death with the manifestations of anaphylactic shock occurring after an injection of penicillin. Despite this isolated report, the great majority of physicians have continued to use penicillin freely in treatment of patients with or without a background of allergic disease. At a recent meeting of the New York Allergy Society, the possible danger of such promiscuous use of penicillin was brought out sharply. Dr. Sheppard Siegal reported three cases of severe immediate reactions of the anaphylactic type following injections of penicillin, one of which proved fatal. The ensuing discussion revealed that the sixty members present had personal knowledge of three other fatal anaphylactic reactions to penicillin, not yet reported in medical journals, and a large number of alarming reactions of the same immediate type in which recovery occurred. The citation of so many cases in a meeting of this size certainly suggests that such immediate reactions, while far less common than the familiar delayed urticarial reactions, are more frequent than the medical literature indicates.

A great majority of the patients cited as having severe immediate reactions of this type gave a past or family history of allergic disease of the hereditary or atopic type; many suffered from asthma. All had received numerous injections of either crystalline or procaine penicillin at irregular intervals, usually for the treatment of recurrent respiratory infections. In some instances, previous injections had caused mild but definite immediate reactions, in others the severe or fatal reaction occurred suddenly after previous doses had been well tolerated. In none of the cases cited had the development of sensitization to penicillin been accompanied by a delayed urticarial reaction similar to serum sickness. All of the fatal reactions followed intramuscular injections, but very severe and equally prompt reactions were reported after instillation of penicillin into the maxillary sinus, inhalation therapy, and oral administration of the drug as tablets. The reactions following the use of crystalline and procaine penicillin were essentially similar, and in no case was there any evidence that the procaine moiety caused the sensitivity. In no instance was there clinical evidence, nor in the two cases coming to autopsy, anatomical evidence, of embolism or other nonallergic cause for the reaction.

Several of the patients who recovered from severe anaphylactic reactions subsequently showed immediate wheal reactions to scratch or intracutaneous tests with penicillin, and in some instances the Prausnitz-Küstner reaction was demonstrable. Intracutaneous tests on some of these patients were followed by severe constitutional reactions. These skin reactions are in striking con-

trast to the negative or questionable results noted in patients with the delayed urticarial type of reaction to penicillin, but consistent with the skin reactions elicited by thiamin, quinine, and occasionally sulfonamides in patients suffering similar anaphylactic reactions from those agents.

While these anaphylactic reactions to penicillin are relatively rare in proportion to the tremendous number of patients treated with the drug, their occurrence, in addition to that far more frequent but less serious delayed urticarial reactions, suggests careful consideration of the repeated use of the drug in patients with allergic diseases. Certainly the occurrence of even a mild immediate allergic reaction after one injection should cause hesitation in repeating the treatment. In most cases one of the other antibiotic agents might be substituted. Use of the arm or thigh rather than the buttocks as the site of injection should lessen the danger by permitting the use of a tourniquet if necessary. The use of penicillin O in patients who had previously received penicillin G might lessen the chance of reaction to a particular dose, but there is no assurance that penicillin O is not an equally active sensitizer if used repeatedly. The combination of penicillin with antihistamine drugs has also been suggested, but the rapidity and severity of the reactions cited raise serious doubt as to whether any reasonable dose of antihistaminic injected simultaneously would have a sufficiently prompt and potent effect to prevent a serious outcome. Since the danger of this type of reaction is becoming apparent only after millions of injections of penicillin have been given over a period of ten years, favorable results in a few hundred cases treated with penicillin-antihistamine combinations have no statistical significance.

The positive reactions to skin tests noted in several of the patients suggest a possible aid in foreseeing and avoiding these reactions. Further studies will be needed to establish the actual value of such tests and to determine a technique of testing which will be sufficiently sensitive to yield reliable results without in itself producing dangerous reactions. Present indications are that scratch tests with solutions containing 10,000 to 50,000 units of crystalline penicillin per millimeter or intracutaneous tests with 0.01 to 0.02 ml. of solutions containing 100 to 1,000 units per milliliter might serve the purpose. Suspensions of procaine penicillin in oil or water are apparently not useful for skin tests.