

History of drug sensitivity in atopic persons

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Seven hundred and forty persons with atopic respiratory disease were interviewed concerning a history of allergic drug reactions. Seventeen per cent gave a positive history, and 90 per cent of the reactions involved the skin. Drug sensitivity occurred most frequently in the third decade of life and in females more than males. The incidence in asthmatic patients was not greater than in patients with only nasal disease. Penicillin was responsible for the reaction in more than one half of the cases, and penicillin, sulfonamides, and aspirin accounted for 80 per cent of the drug reactions. Of those persons with a history of drug allergy, 9.4 per cent had sensitivities to two or more drugs.

It has been suggested that allergic reactions to drugs occur more frequently in atopic persons.^{1, 2} Although this may be based on clinical impression rather than statistical data,³ the atopic patient often gives a history of sensitivity to a drug that would otherwise be beneficial to him. The history of the past reaction, although frequently questionable, is usually the basis for a clinical diagnosis of drug allergy. Skin testing to drugs as penicillin and basophil degranulation studies may be useful in certain cases, but they frequently are not conclusive.

Our purpose was to study the histories of drug sensitivities in atopic persons. We wished to determine the frequency of the drug sensitivities, the drugs involved, the type of reaction, and characteristics of the atopic individual involved.

METHOD

Seven hundred and forty persons with atopic respiratory disease were interviewed by the author concerning the history of drug allergies. Patients with eczema or urticaria without atopic respiratory disease and patients who were referred specifically because of a drug reaction were not included.

The study was purely clinical. No diagnostic evaluation to confirm the drug allergy was attempted. The criteria for a positive history were the appearance of a large local reaction, urticaria, angioedema, skin eruption, rhinitis, asthma, or shock following the administration of a drug. A history that was considered

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positive would deter the author from prescribing the drug again except possibly under very unusual circumstances.

The following information was obtained from each patient: age, sex, drug or drugs involved, type of reaction, and age at the time of the reaction. The patients were placed into one of three categories of atopic disease after appropriate evaluation: (1) pure seasonal pollinosis, (2) perennial allergic rhinitis, or (3) perennial allergic rhinitis and bronchial asthma.

RESULTS

Of the 740 patients with atopic respiratory disease, 127 (17 per cent) had a positive history of drug allergy. The mean age of all the patients was 29 years, with a range of 2 to 71 years. The mean age at the time of the drug reactions was also 29 years, with the range being 1 to 62 years.

Table I. *Type of drug reactions*

<i>Clinical manifestations</i>	<i>No. of patients</i>
Urticaria and/or angioedema	81
Skin rash	34
Local reaction	13
Asthma	12
Rhinitis	1
Shock	1

Table II. *Drugs responsible for the allergic reaction*

<i>Drug</i>	<i>No. of cases</i>
Penicillin	78
Sulfonamides	19
Acetylsalicylic acid	17
Codeine	5
Terramycin	3
Streptomycin	2
Chloromycetin	2
16 other drugs	1 each

Table III. *Type of penicillin reaction and age at time of reaction*

<i>Reaction</i>	<i>Age of patients (years)</i>						
	<i>0-10</i>	<i>11-20</i>	<i>21-30</i>	<i>31-40</i>	<i>41-50</i>	<i>51-60</i>	<i>61-70</i>
Local reaction	1	0	4	5	2	0	0
Skin rash	10	3	3	3	1	1	1
Urticaria and/or angioedema	8	5	14	6	4	4	2
Shock	0	0	0	0	1	0	0

Four hundred (54 per cent) of the patients were female. Of those with a history of drug allergy, 83 (65 per cent) were female.

The clinical manifestations of the drug reactions are summarized in Table I. There were 142 drug reactions in the 127 patients with 90 per cent of the reactions involving the skin. There was no significant difference in the incidence of drug allergies in the three categories of atopic disease.

Of the 142 drug reactions, 78 (55 per cent) were due to penicillin. Eleven per cent of all the atopic persons gave a history of penicillin allergy. Sulfonamides were responsible for 19 reactions and acetylsalicylic acid (aspirin) for 17. These 3 drugs were incriminated in 80 per cent of all the cases. Table II lists the drugs believed to have produced the 142 allergic reactions.

The penicillin drug reactions may be further analyzed. Urticaria and/or angioedema occurred in 43 patients, skin rash in 23, large local reactions in 11, and shock in 1. Forty-eight (62 per cent) of the patients were female. The type of penicillin reactions occurring in the different age groups is listed in Table III.

The drug responsible for the respiratory symptoms was acetylsalicylic acid. Rhinitis was produced in 1 patient, and asthma occurred in 12. Angioedema also occurred in 2 of the latter patients and in 4 others without associated respiratory symptoms. Ten of the 12 who had aspirin-induced asthma had large nasal polyps, and 11 of the 17 aspirin-sensitive patients were female.

Of the 127 patients with a history of drug allergy, 12 (9.4 per cent) had reactions from 2 or more drugs. Ten of the 12 were sensitive to penicillin, and 4 had sulfonamide sensitivity.

DISCUSSION

Any study that relies entirely upon the history of the patient is subject to error. This is especially true when the event may have occurred 10 to 15 years previously. However, in most instances, it was not difficult to determine whether the untoward reaction was that of idiosyncrasy, intolerance, pharmacologic effect, secondary to abnormal bacterial or mycotic overgrowth, or by our criteria, allergic. There may be disagreement concerning our criteria for an allergic reaction, but these are usually accepted. Urticaria from codeine was accepted and folliculitis from iodides was not, although both these eruptions may be due to pharmacologic action rather than allergy. The skin rash in youngsters that follows the use of an antibiotic was certainly the most difficult to establish as an allergic reaction. The rash may have been due to the disease rather than medication. Despite these deficiencies, it is the history that the clinician usually relies upon in the problem of drug allergy.

Young children have been reported to develop penicillin sensitivity at a lower rate than adults.⁴ Our study does not suggest this difference, but this may be due to the misinterpretation of the skin rash following penicillin administration and the frequent use of the drug in children. Urticaria and angioedema due to penicillin occurred most frequently in the third decade of life, but the first decade followed. The greatest number of all drug reactions also occurred in the third decade.

Eleven per cent of all the atopic patients gave a history of penicillin allergy. This is slightly higher than an estimate of 2 to 8 per cent reaction rate in all persons receiving penicillin.⁵ Smith and associates² found that men were more likely to develop penicillin reactions than were women. Females comprised 62 per cent of our patients with a history of penicillin sensitivity although they made up only 54 per cent of the entire group.

Acetylsalicylic acid was the only drug that produced definite respiratory symptoms. There were 12 cases in which asthma occurred, usually in about 10 to 20 minutes after taking the tablet. The asthma was often severe and difficult to relieve. Ten had asthma at other times, but 2 did not. Ten also had large nasal polyps, and this association has been noted previously.^{6, 7} There were 36 patients with large nasal polyps, and 13 had an allergy to some drug. In our particular group, 20 of the 36 patients with nasal polyps also had bronchial asthma.

A history of sulfonamide sensitivity was present in 2.6 per cent of the patients. The reactions frequently had occurred many years ago, and the history was often somewhat vague. In two instances, skin eruption had occurred after taking sulfonamides 15 to 20 years ago but not after receiving one of the newer sulfonamide preparations more recently.

The remainder of the drugs believed to be responsible for allergic reactions included antibiotics, narcotics, local anesthetics, tranquilizers, and injected thiamine.

The greatest drug exposure would be expected in the patient with perennial asthma. However, the incidence of drug sensitivity was not significantly different in the asthmatic than in patients with perennial rhinitis or seasonal pollinosis. The patient most likely to have an allergic skin eruption (Mrs. Iva Rash) had none.

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