

THE PREVALENCE OF RAGWEED POLLINOSIS IN FOREIGN AND NATIVE STUDENTS AT A MIDWESTERN UNIVERSITY AND ITS IMPLICATIONS CONCERNING METHODS FOR DETERMINING THE INHERITANCE OF ATOPY

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NUMBERS of investigators have attempted to define the inheritance of atopy. Isolated family pedigrees,¹⁻¹² twin studies,¹³⁻¹⁹ and multiple case studies¹⁹⁻²⁸ have been employed for this purpose. At present there is fairly general agreement that the former type of data are unsuitable for evaluating the heredity of diseases of such common occurrence as atopic disorders, and conflicting conclusions have been reached from studies of the latter two types. The many factors which may have contributed to these discrepancies have been reviewed by Schwartz,²⁶ Dahlberg,²⁹ DeGara,³⁰ and others.³¹⁻³³ Prominent among these is the probability that the development of clinically overt atopic disease is conditioned by exposure to potent environmental allergens as well as by hereditary factors. If this is true, past and continuing attempts to define the inheritance of atopy purely by the multiple case study approach are likely to be inconclusive. This report attempts to document this contention by surveying the personal and familial prevalences of some clearly defined atopic diseases occurring among foreign and native students in an area where there is an abundance of a potent allergen (ragweed pollen) not present in most other countries. There is shown to be a significant difference in the onset and familial history of atopy between these two groups of patients suffering from the same diseases. The study also provides data about the prevalence of atopy in various nationality groups and among native university students residing in an area having relatively large amounts of tree, grass, and weed pollens and fungus spores in the air.

METHODS

The survey was accomplished by means of a comprehensive, 8-page questionnaire which elicited such information as the student's age, racial ancestry, time of arrival in the United States and Michigan, age of onset and type of any

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allergic symptoms, exact seasonal occurrence of symptoms, a detailed family history of allergy and previous treatment. Past as well as current symptoms were included, the results of this survey thus indicating a "cumulative prevalence." The 322 University of Michigan foreign students who were studied were selected, in 1960, from a total group of 985 foreign students on the campus solely on the basis of previously known good comprehension of English, ready accessibility through nationality organizations, and exclusion of persons from southern Canada. These foreign students were approached in small groups of 10 to 20 persons. Before they began to answer the questionnaire, each of the allergic entities being evaluated was explained by one of the investigators, and a description of the atopic diseases was repeated in writing on the questionnaire. When in doubt concerning the answers to certain questions, the students were encouraged to indicate uncertainty rather than to guess. The questionnaires were briefly reviewed with each student as they were turned in. The relatively few questionnaires which were unsatisfactory because of incompleteness or marked uncertainty were excluded from the analysis of the data.

The control groups of native American students are outlined in Table I.* The questionnaires were reviewed with each of the unselected native student controls. Additional information also was obtained by the same questionnaire but without personal contact from medical and nursing students and known atopic patients, but, unless otherwise indicated, only the data obtained from the unselected native students were used in the following analysis of the results. In a further effort to focus upon items of data which are most likely to be reliable, only allergic rhinitis and/or extrinsic or mixed intrinsic and extrinsic bronchial asthma were included as "atopic disease" in this paper.† Likewise, only the occurrence of allergic rhinitis or bronchial asthma (any type) in a parent or sibling was considered a positive family history of "atopy" in this study.

TABLE I. STUDENTS SURVEYED

GROUP	NO.	MEDIAN AGE	% MALE
Foreign students	322	25 yr.	82
Unselected native students	434	20 yr.	62
280 dormitory students			
154 transferring or entering students seen during registration			
Second year medical and nursing students	205		
Atopic patients from the Student Health Service Allergy Clinic	162		
Total group	1,123		

RESULTS

Table II shows the prevalence of ragweed pollinosis, personal atopy, and familial atopy in some of the major nationality groups surveyed. The number

*Although the unselected native student controls were younger than the foreign students and more were female, it was found that within this native student control group there were no significant differences in the prevalence of ragweed pollinosis between males and females or between students with a median age of 20 years and those with a median age of 25 years.

†It is not implied that we necessarily regard these as the only atopic diseases, but it was believed that the reliability of the data would be compromised by trying to identify other atopic conditions by means of a questionnaire.

of students in these individual groups is too small and their length of residence in Ann Arbor too variable to warrant any conclusions about relative prevalence rates among these groups, but it is evident that these conditions do occur in many nationalities.

TABLE II. FOREIGN STUDENTS SURVEYED

NATIVE LAND	TOTAL NO.	NO. WITH RAGWEED POLLINOSIS	NO. "ATOPIC"	NO. WITH FAMILIAL ATOPY
India and Pakistan	90	5 (6%)	16 (18%)	13 (14%)
China	75	12 (16%)	17 (23%)	12 (16%)
Philippines	40	3 (8%)	7 (17%)	6 (15%)
South America (11 countries)	43	3 (7%)	7 (16%)	8 (16%)
Near East (Turkey, Iran, Iraq)	41	5 (12%)	8 (20%)	7 (17%)
Western Europe	12	3 (25%)	4 (33%)	3 (25%)
Eastern Europe	9	3 (33%)	3 (33%)	2 (22%)
Miscellaneous	12	4 (33%)	6 (50%)	3 (25%)

Table III shows the comparative prevalence of ragweed pollinosis and atopy in the foreign and native students. The differences between the two groups are not significant by the chi-square test. It is of interest that the medically oriented control group showed a higher prevalence of ragweed pollinosis and "atopy" than the control group from the student body at large, but the difference was not significant.

TABLE III. PREVALENCE OF RAGWEED POLLINOSIS AND "ATOPY" IN FOREIGN AND NATIVE STUDENTS

GROUP	NO.	RAGWEED POLLINOSIS	"ATOPY"
Foreign students	322	38 (12%)	68 (21%)
Foreign students in U. S. A. 2 or more R. W. seasons	190	34 (18%)	
Unselected native students	434	67 (15%)	83 (19%)
Second year medical and nursing students	205	35 (17%)	50 (24%)

Table IV shows a marked discrepancy in the presence of familial "atopy" in the groups under comparison. The "atopic" foreign and native students differ in regard to the occurrence of familial atopy at the 1 per cent level of significance, and the students with ragweed pollinosis differ at the 2 per cent level of significance.

TABLE IV. FAMILIAL ATOPY

GROUP	NO.	POSITIVE FAMILY HISTORY OF ATOPY
Foreign students with personal atopy	68	22 (33%)
Foreign students with ragweed pollinosis	38	14 (36%)
Native students with personal atopy	89	55 (62%)
Native students with ragweed pollinosis	67	42 (63%)
Native allergic Student Health Service patients	170	109 (64%)

Table V shows a large difference between the foreign and native student groups in regard to the initial onset of ragweed pollinosis during their college

years. It is evident that during their second to fifth ragweed seasons in the United States, the onset of ragweed pollinosis occurred more than 10 times more frequently among foreign students than among natives of the same age, a difference which is significant at the 1 per cent level. Naturally, the foreign students could not have developed ragweed pollinosis at a younger age, since they were not exposed to the allergen, but the fact that the large majority of native students developed their ragweed symptoms at an earlier age illustrates the role of the environment in determining the time of onset of the disease.

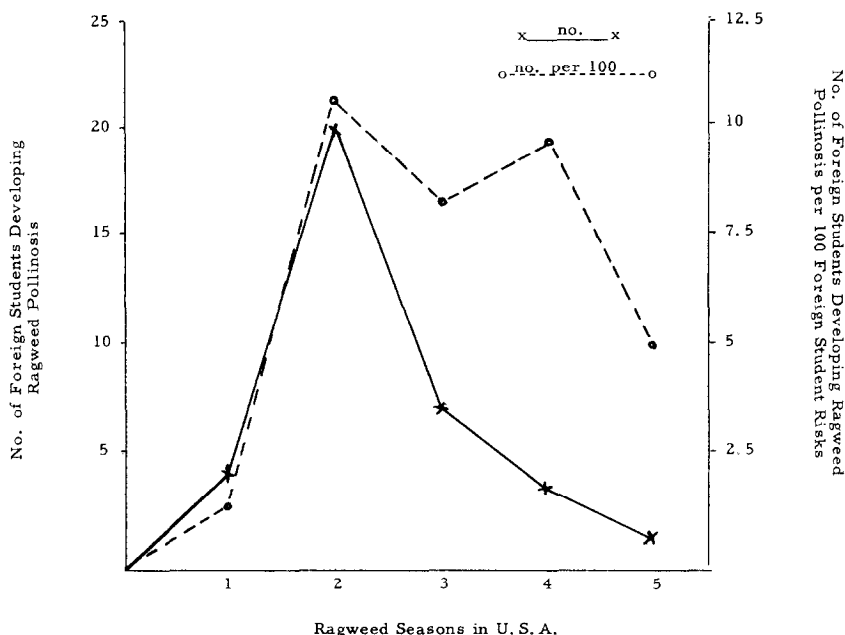


Fig. 1.—Time of onset of ragweed pollinosis in foreign students.

TABLE V. INITIAL ONSET OF RAGWEED POLLINOSIS DURING COLLEGE YEARS

	NO. OF STUDENTS	INITIAL ONSET OF RAGWEED POLLINOSIS
Onset of ragweed pollinosis in foreign students residing 2 to 5 ragweed seasons in U. S. A.	161	31 (19%)
Onset of ragweed pollinosis in native students of similar age	123	2 (1.6%)

Fig. 1 depicts the number of foreign students developing ragweed pollinosis according to years of residence in the United States. Although a large portion of the students developed symptoms during the second ragweed season, this observation is influenced by the fact that a substantial part of the foreign student group had been in residence only 2 years. Thus, the dashed line, indicating the number of cases of ragweed pollinosis developing per 100 foreign student risks,* gives a more valid representation of the latent period in the development of ragweed pollinosis.

*By foreign student risks is meant the number of foreign students in residence the indicated number of ragweed seasons who had not developed ragweed pollinosis in previous years.

In view of our finding more familial atopy in the native than foreign students afflicted with atopy or ragweed pollinosis, the possibility was considered that atopy or ragweed pollinosis might not be influenced at all by inheritance³¹ or that the mode of inheritance might be different in the foreign and native student groups. The latter possibility seemed very unlikely, however, in view of the fairly similar prevalences of familial allergy in all foreign national groups studied, including Europeans. The data presented in Table VI reaffirm the probability that heredity plays some role in the pathogenesis of ragweed pollinosis. The observed differences in the prevalence of this condition between groups with positive and negative histories of personal or familial atopy are significant at the 1 per cent level in regard to the native students. Table VII provides further confirmatory evidence that ragweed pollen is no more capable of eliciting atopic hypersensitivity in unpre-disposed persons than is another group of common allergens, the grass pollens. It is seen that ragweed pollinosis occurs with substantially no relatively greater frequency than grass pollinosis among persons with negative family histories of atopy when compared to students with positive family histories.

TABLE VI. RELATIONSHIP OF PERSONAL AND FAMILIAL ATOPY TO THE PREVALENCE OF RAGWEED POLLINOSIS

	PORTION OF STUDENTS WITH RAGWEED POLLINOSIS		
	FOREIGN	NATIVE	TOTAL
Personal history of other atopic disease	22/47 (47%)	44/70 (63%)	66/117 (56%)
No personal history of other atopic disease			
Positive family history of atopy	8/30 (27%)	12/90 (13%)	20/120 (17%)
Negative family history of atopy	8/245 (3.3%)	11/274 (4.0%)	19/519 (3.7%)
Total group	38/322 (11.8%)	67/434 (15.4%)	105/756 (13.9%)

TABLE VII. THE RELATIVE FREQUENCY OF RAGWEED AND GRASS POLLINOSIS AMONG STUDENTS WITH POSITIVE AND NEGATIVE FAMILY HISTORIES OF ATOPY

	NEGATIVE FAMILY HISTORY	POSITIVE FAMILY HISTORY	TOTAL CASES (NATIVE AND FOREIGN STUDENTS)
Ragweed pollinosis	47/596 (7.9%)	58/160 (36%)	105/756 (13.9%)
Grass pollinosis	32/596 (5.4%)	41/160 (26%)	73/756 (9.7%)

Therefore, the ratio of

ragweed cases/grass cases with a negative family history equals $47/32 = 1.47$

ragweed cases/grass cases with a positive family history equals $58/41 = 1.41$

Table VIII shows the prevalences of allergic rhinitis and bronchial asthma among the 434 unselected native student controls. It is of interest that whereas 25 of 83, or 30 per cent, of these "atopic" students had experienced bronchial asthma, 44 per cent of the 162 surveyed atopic patients who sought treatment at the Student Health Service Allergy Clinic had had bronchial asthma. Also, as shown in Table IX, 24 per cent of the allergic rhinitis patients seen at the Student Health Service developed bronchial asthma subsequent to the onset of their allergic rhinitis, while this sequence of events occurred in only 9 per cent

of the unselected native students. Although these differences are significant at only the 5 per cent level in this rather small series of cases, they should serve as a reminder that statistics obtained from atopic patient populations are not necessarily representative of all atopic persons in the community at large. The data suggest that physicians tend to see a selected group of atopic persons who have the more severe forms of atopic disease. The foreign students tended to have bronchial asthma in association with their ragweed pollinosis more often than the native students, but the difference was not significant.

TABLE VIII. PREVALENCES OF ALLERGIC RHINITIS AND BRONCHIAL ASTHMA AMONG THE 434 UNSELECTED NATIVE STUDENT CONTROLS

NO. OF STUDENTS	MANIFESTATION OF ATOPY	PERCENTAGE OF TOTAL STUDENTS
83	"Atopic"	19.1%
58	Allergic rhinitis alone	13.4%
14	Allergic rhinitis and bronchial asthma	3.2%
11	Bronchial asthma alone	2.5%
		16.6%
		5.7%

TABLE IX. TEMPORAL RELATIONSHIPS IN THE ONSET OF ALLERGIC RHINITIS AND BRONCHIAL ASTHMA

	UNSELECTED NATIVE STUDENTS	STUDENT HEALTH SERVICE PATIENTS
Allergic rhinitis alone	58	87
Allergic rhinitis and bronchial asthma		
Bronchial asthma first	3	6
Approximately simultaneous onset of allergic rhinitis and asthma	5	9
Allergic rhinitis first	6	27
Temporal relationship uncertain	0	20
Portion of allergic rhinitis patients subsequently developing bronchial asthma	6/64 (9%)	27/114 (24%)

DISCUSSION

The data presented in Table IV support the contention that the family history is not a reliable criterion for establishing the inheritance of atopy, for here are two groups of persons afflicted with the same allergic diseases in the same community but having significantly different family histories. In part this difference may be attributed to poorer recognition of atopic disease in members of their families by the foreign students due to less familiarity with these entities. However, we believe that this is not the major factor explaining this difference. Because of the selection of students with a good comprehension of English and the verbal and written description of the atopic diseases provided to them, the foreign students appeared to have a good understanding of the information desired of them and completed their questionnaires carefully; only persons who had been able to recognize atopic disease *in themselves* are being compared in Table IV, and it would be expected that these individuals could recognize atopic disease among their relatives,¹⁹ even retrospectively, more readily than the average foreign student; and by limiting the analysis of the data to parents and siblings, the reliability of the family histories should have

been enhanced. Thus, there is reason to believe that the difference in familial history of atopy is not due entirely to reporting errors, but even if it were, the limitations of the family history would be demonstrated. Although Smith³⁴ has suggested that the allergic diathesis is infectious, the most usual explanation for this difference is that latent atopy is present in the families of many of these foreign students but does not result in clinically overt atopic disease until some member of the family is exposed to a potent allergen such as ragweed pollen. In this regard, it is notable that 23 of the 38 foreign students developing ragweed pollinosis had no "atopic" symptoms in their homelands.

These data are remarkably similar to the observations of Shilkret and Lazarowitz³⁵ on hay fever among immigrants. They found that only 22.5 per cent of 162 immigrant hay fever patients had a familial history of allergy, while 51 per cent of 102 American born controls gave a positive family history. Only 19 per cent of the immigrants had a personal past history of allergy. Fine and Abram³⁶ reported that 29 per cent of 32 immigrant hay fever patients gave a history of familial allergy.

The rather explosive onset of ragweed pollinosis among our foreign students, illustrated in Table V, also is most easily explained by the hypothesis that the foreign student group includes a reservoir of latent atopy which does not manifest itself until the students are exposed to the potent ragweed allergens. The type of analysis used in Table V is especially appealing in that it only requires the surveyed person be able to recognize symptoms of ragweed pollinosis *in himself*.

Our data regarding the time of onset of ragweed pollinosis (Fig. 1) are quite similar to the observations of Piness and Miller³⁷ on the onset of pollinosis among new arrivals in two isolated mining communities. Studies of immigrants,^{35, 36, 38, 39} however, have generally shown a considerably longer "incubation period" in the development of pollinosis. The fact that all ages were included in these foreign born groups may in part explain the differing results, since it might be expected that foreign born children and perhaps older adults would have a longer "incubation period" than our college student age group. As indicated below, it also appears that there are differences between college students and the general populace in regard to the occurrence of atopic disease.

One of the most striking incidental findings of this study is the extremely high prevalence of ragweed pollinosis and atopy in all the student groups surveyed. Although the prevalences are much higher than ordinarily reported for entire populations, the data are more nearly in agreement with some other surveys of *student* groups. It is difficult to make precise comparisons with reports in the literature because of variable criteria for a diagnosis of "atopic" disease, but Table X shows approximately the reported prevalences of bronchial asthma and allergic rhinitis in various university student surveys. There are many factors which may account for the marked variability in the results of these surveys. Among these are the definition of and criteria for the diagnosis of atopic disease, care in the construction of questionnaires, number of questions asked, the method of collecting the data, selection of persons being surveyed, differing locales of the studies, inclusion of past symptoms as well as current

difficulty, general intelligence of those being interviewed, the probable spread of ragweed in recent decades, and increasing general awareness of the atopic diseases. The latter may perhaps in part account for the apparent trend toward higher prevalences with the passing decades. It is of interest that Tips' results at the University of Notre Dame²⁷ are almost identical to ours, and this survey was conducted in recent years in an area with similar vegetation. The high prevalence recently reported by Van Arsdel and Motulsky²⁸ also is of interest in view of the fact that they work in an essentially ragweed free area. Data obtained under less critical conditions from 1,861 students at our own institution in 1953 yielded even higher prevalences of allergic rhinitis and bronchial asthma than the results reported in this paper.⁴² Using a much broader definition of allergy, Kalliola, Kasanen, and Peltonen⁴³ found "academic persons" and student nurses to be afflicted far more frequently than other segments of the populace in southwest Finland. Haynal⁴⁴ found a statistically significant difference in the prevalence of hay fever (but not asthma) in the families of 16-year-old school children in Zurich according to social class, the upper classes being most afflicted.

TABLE X. REPORTED PREVALENCE OF BRONCHIAL ASTHMA AND ALLERGIC RHINITIS IN UNIVERSITY STUDENT POPULATIONS

YEAR	INVESTIGATORS	PLACE OF SURVEY	PREVALENCE OF ASTHMA AND ALLERGIC RHINITIS AMONG STUDENTS
1924	Spain and Cooke ²⁰	New York	3.3%
1930-34	Jimenez ⁴⁰	Michigan	12%
1937	Rowe ⁴¹	California	10-13%
1932-50	Ratner and Silberman ²⁵	New York	10-13%
1954	Tips ²⁷	Indiana	18.7%
1959	Van Arsdel & Motulsky ²⁸	Washington	16.7%
1960	Present study	Michigan	19.2%

It seems clear, therefore, that the reported prevalence of atopic disease is substantially higher in university students in recent years than the prevalence usually quoted for the general population. Although a consideration of the general prevalence of atopy is beyond the scope of this report, it is pertinent to consider whether this difference between the students and the general population is real or only apparent. If the latter (e.g., due to students' increased awareness of the atopic diseases), it follows that the usual estimates of the general occurrence of atopic disease probably are substantially too low, particularly if "cumulative prevalence" is being considered.* If the difference in the occurrence of atopic disease between students and the general populace is real, it would be highly desirable to ascertain the factors associated with and responsible for this difference. Intelligence⁵ and emotional stress⁴⁵ have been suggested as possibilities. Unfortunately, however, there does not appear to be any information which indicates whether the increased reported prevalence of atopic disease among university students is real or artifactual.

*By "cumulative prevalence" is meant the past or present occurrence of a disease. This could not possibly decrease with age, and, since students are younger than the median age of the populace, it would be expected that the true "cumulative prevalence" would be higher for the general population than for students. The only exception to this expectation would arise from a real difference in the occurrence of atopy in different generations.

There are major limitations to any conclusions which can be drawn from surveys of the inheritance and prevalence of atopic disease, since in effect these require people to diagnose allergy in themselves and their relatives. Objections have been raised to the use of questionnaires in these surveys,²⁵ but it was hoped that the supplementary personal contact employed in our study would enhance the validity of the data. For obvious reasons it was impossible for us to obtain information directly from these students' relatives, and unfortunately it also was not feasible to skin test the groups under study. However, since some of our foreign students and native student controls were seen, by chance, as patients at the Health Service Allergy Clinic, it was possible in these instances to compare the questionnaire information with conclusions reached following a complete allergy evaluation, including skin testing. Of 19 students judged to have ragweed pollinosis by questionnaire, the "diagnosis" was confirmed in 17 instances by a complete history and skin tests. Similarly, in the 16 instances where adequate information concerning the family history of allergy was available from the Health Service record, it confirmed the questionnaire in 15 cases. In 13 of 15 cases there was agreement (within one year) in regard to the age of onset of symptoms. Nevertheless, it seems likely that it will not be possible to delineate the role of inheritance or the prevalence of the atopic state until a simple, reliable objective test for atopy is devised. Until such a test is available, epidemiologic studies are likely to contribute to an understanding of these problems in proportion to the care with which the data are collected. A conservative interpretation of what can be accepted as atopic disease on the basis of survey methods also appears to be desirable.

CONCLUSIONS

1. Ragweed pollinosis and other atopic diseases occur in many nationality groups.
2. Data are presented which strongly suggest that exposure to potent environmental allergens, as well as inheritance, affects the prevalence and onset of clinically overt atopic disease. Although this conclusion may appear obvious to the clinical allergist, it seemed worth while to take advantage of the rather unique opportunity afforded by our foreign student population to try to document previous clinical impressions.
3. The apparent prevalence of atopic disease in university student populations is substantially higher than the prevalence generally reported for the general populace.
4. Data obtained from atopic *patient* populations may differ from observations on unselected atopic persons in the community at large.

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