

Melon and banana sensitivity coincident with ragweed pollinosis

L. Bruce Anderson, Jr., M.D.,* Eric M. Dreyfuss, M.D.,
Jonathan Logan, M.D., Douglas E. Johnstone, M.D., and
Jerome Glaser, M.D., Rochester, N. Y.

Because of a suspected relationship between ragweed pollinosis and melon or banana sensitivity, 2,067 consecutive patients in an allergy practice were queried with regard to symptoms from melon or banana ingestion. Of 1,447 patients with pollinosis, 90 complained of oral pruritus, which was by far the most common symptom caused by these fruits. No melon- or banana-induced oral pruritus occurred in any of 620 allergic patients who did not have pollinosis. Melon- or banana-sensitive patients as a group showed the following characteristics: (1) All were sensitive to ragweed or grass pollen clinically and by skin test. (2) Most showed a much higher degree of skin test sensitivity to ragweed than a control group of patients with ragweed pollinosis who were not melon or banana sensitive. (3) The prevalence of asthma was much higher in the melon- and banana-sensitive group (78 per cent) than that in the control group (47 per cent). Immunologic studies with rabbit antisera showed no common antigens by Ouchterlony gel diffusion between ragweed, melon, and banana or between timothy, melon, and banana, although common antigens were found between all of the melons, (watermelon, cantaloupe, and honeydew). Passive cutaneous anaphylaxis in guinea pigs demonstrated a strong cross-reaction between ragweed antigen and cantaloupe antibody, suggesting common antigenic determinants as an explanation for the melon sensitivity-ragweed pollinosis syndrome. Possible alternative causes of this relationship are discussed.

Patients with hay fever frequently complain of oral pruritus from eating melons, but very little has been written about this common association. Sheldon and associates¹ briefly commented on melon sensitivity in ragweed pollinosis patients. Scott and Epps² noted oral pruritus from food coincident with pollinosis but did not specify which foods. Pisani and associates³ reported multiple cross-sensitivities between foods and pollens without mentioning symptoms. Mallet⁴ reported asthma from eating cantaloupe purportedly due to a contaminating yeast, and cantaloupe has been implicated in allergic purpura,⁵ but there is little else in the literature regarding sensitivity to melons.

From the Department of Pediatrics, University of Rochester School of Medicine and Dentistry.

Received for publication July 19, 1969.

*Reprint requests: 2802 Ninth Avenue North, Billings, Mont. 59103.

The frequency of melon-induced oral pruritus in Rochester, New York, hay fever patients focused our attention on this syndrome, and we soon became aware of the fact that banana was also causing symptoms almost as often as melon. Other foods were mentioned by patients with pollinosis but not nearly as frequently. A review of the literature failed to reveal any additional specific information (aside from the fact that the subject heading "Fruit" is followed immediately by "Frustration" in the *Quarterly Cumulative Index*).

This apparent cross-sensitivity between three biogenetically unrelated plant allergens prompted a survey of allergic office patients in the further investigation of this subject.

METHODS

Melon and banana sensitivity survey

Patient interviews. All patients seen by us in an allergy practice between July, 1968, and February, 1969, were interviewed with the use of a standard questionnaire. Each was queried regarding food intolerances, and if no spontaneous responses were forthcoming, then melon, banana, grape, and pineapple were specifically mentioned; the latter two fruits were chosen as controls, pineapple in particular because of its sharp taste and because of the fact that it contains serotonin in appreciable amounts, as does banana.^{6, 7, 8}

Skin tests. Patients were skin tested only as indicated by their clinical symptoms. Our procedure included scratch tests with ragweed and mixed grass extracts, 1:50. If a reaction was less than 2+, then intradermal skin tests with extract dilutions of 1:500 and 1:100 (if still less than 2+) were performed. Strongly positive scratch tests were titrated by scratches with extract dilutions of 1:12,500 and 1:62,500. A few patients were scratch tested with melon and banana fresh frozen homogenate and some with glycerine extract 1:50, but this was not done routinely.

Immunologic studies

Agar gel diffusion. Rabbits were injected with antigen in Freund's complete adjuvant intradermally in multiple sites. Antigens used were banana (9,000 PNU per milliliter), watermelon (20,000 PNU per milliliter), honeydew melon (20,000 PNU per milliliter), cantaloupe (20,000 PNU per milliliter), whole ragweed extract (65,000 PNU per milliliter), and timothy (65,000 PNU per milliliter). A second set of injections with the same materials was given at 14 days, followed by daily intravenous doses of alum-precipitated antigen from Days 21 to 28. Sera were obtained at 35 days and again at 42 days and tested for the presence of antibody by Ouchterlony gel diffusion against multiple dilutions of antigen. Each antiserum was then diffused against optimal dilutions of each antigen to determine the presence of cross-reactivity.

Passive cutaneous anaphylaxis. Albino guinea pigs were passively sensitized, in duplicate, intradermally with rabbit antisera according to the method of Ovary.⁹ Each animal received either ragweed or timothy antisera as well as banana or one of the melon antisera. All antisera were injected full strength and in dilutions of 1:10 and 1:100. Each animal was also injected with normal

rabbit serum as a control. Four hours later, one of each pair was challenged intravenously with either ragweed or timothy antigen and the other with either banana or melon antigen, in each instance mixed with Evans blue dye.

RESULTS OF PATIENT SURVEY

During the 7 month period of the survey, 2,067 allergic patients were interviewed, of whom 1,447 (70 per cent) had pollinosis listed as at least one of their diagnoses. Among these, 86 patients had characteristic oral pruritus from eating melon and/or banana. Four other patients, in addition, had related oral symptoms (sore mouth with aphthous ulcer—2; hoarse voice—2), bringing the total to 90. The incidence of this syndrome was 4.3 per cent of all patients interviewed and 6.2 per cent among patients with pollinosis. All 90 cases were found to be clinically sensitive to ragweed as their predominant problem, and all had positive skin tests to ragweed. Since many of the 1,447 pollinosis patients had other allergic problems as their primary difficulty, with pollinosis only an

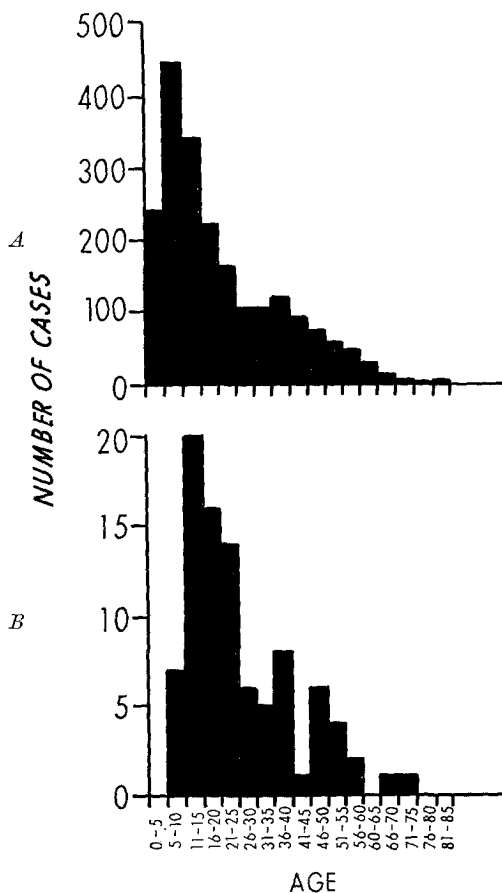


Fig. 1

A, Age distribution of patient population studied (2,067). *B*, Age incidence of MB-sensitive patients (90).

incidental finding, the incidence is probably much higher among patients whose major complaint is ragweed hay fever. Among 620 patients without pollinosis we were unable to elicit a history of oral symptoms from melon or banana ingestion.

Fig. 1 shows the age distribution of the interviewed patients compared with the age incidence of the melon-banana (MB)-sensitive group. No cases of the syndrome were found in patients under the age of 8, although there were more patients in this general age group (6 to 10 years) than any other age group interviewed. Otherwise the age of MB-sensitive patients parallels closely that of the patient population interviewed, with the peak incidence in the 11 to 15 age group and continuing with a high morbidity rate through age 25. This, of course, merely reflects the particular practice interviewed. It is probable that the age incidence of MB sensitivity is very similar to that of pollinosis in general. There was no marked sex difference, although females were found to be MB sensitive more frequently (60 per cent) despite a preponderance of males in the group interviewed (54 per cent).

The character and frequency of specific symptoms from eating melon or banana are shown in Table I. Oral pruritus occurred almost 5 times more often than any other complaint. Melon (cantaloupe, watermelon, and honeydew) elicited symptoms almost twice as often as banana, but the two were mentioned together so frequently (28 out of 89) as to suggest a more than casual relationship. The prevalence of oral sensitivity to all other foods is shown in Table II. Most other foods causing an itching throat did so in patients who were also MB sensitive. Only 9 patients without MB sensitivity complained of an itching throat from other foods. All the foods listed produced oral pruritus only in an uncooked state with the exception of lemon drops, licorice, fish, and chocolate. A few patients with MB sensitivity had oral pruritus from ingestion of these fruits only during the pollen season, but most had difficulty throughout the year.

Melon- and banana-induced oral pruritus seems to be a valid symptom,

Table I. *Symptoms from eating melon and/or banana*

<i>Symptoms</i>	<i>No. of patients</i>	<i>Banana</i>	<i>Melon</i>	<i>Both</i>
Itching throat	89	15	46	28
Gassiness and indigestion	18	5	7	6
Cramps and diarrhea	12	5	2	5
Sore mouth or tongue, canker sores	7	1	6	0
Swollen lips	7	4	1	2
Wheezing	3	2	0	1
Hoarseness	3	1	0	2
Urticaria-angioedema	3	1	2	0
Itching ears	3	0	3	0
Vomiting	3	1	2	0
Nasal congestion	3	0	2	1
Rash	2	1	1	0
Swollen throat	1	0	1	0
Headache	1	0	1	0
Flare of eczema	1	0	1	0
Itching hands	1	0	1	0

Table II. *Frequency of oral pruritus caused by food*

Cantaloupe	74	Pineapple	4	Cottonseed flour	1
Watermelon	50	Raw potato	3	Onion	1
Banana	47	Strawberry	3	Lemon drops	1
Honeydew melon	35	Peas	3	Avocado	1
Citrus fruit	14	Plums	3	Licorice	1
Unpeeled peach	11	Cheese	2	Buckwheat	1
Tomato	8	Lettuce	2	Filbert	1
Celery	6	Pecan	2	String bean	1
Walnut	6	Almond	2	Artichoke	1
Cucumber	5	Fish	2	Conconut	1
Pear	5	Raw cabbage	2	Apricot	1
Green pepper	4	Cherry	1	Berry	1
Apple	4	Spinach	1	Chocolate	1
Grape	4				

despite the fact that these fruits were specifically named as a leading question when patients did not volunteer this information during the survey. Melon and/or banana were named 206 times by 86 patients, while the control fruits, grape and pineapple, elicited a similar response only 8 times by 8 patients.

Analysis of skin tests

As previously noted, every patient complaining of oral pruritus from ingestion of melon or banana was also sensitive to ragweed both clinically and by skin test. Comparison of ragweed skin tests of MB-sensitive patients to those of randomly selected non-MB-sensitive ragweed pollinosis patients shows a definite difference. As shown in Fig. 2, the MB-sensitive group demonstrated a much greater skin test reactivity to ragweed than did the control group. No attempt was made to assess either group for degree of severity of pollinosis symptoms. All patients were considered clinically ragweed sensitive on the basis of typical pollinosis symptoms during the weed pollen season in Rochester, New York (mid-August until late September). Scratch tests for melon and banana sensitivity were done on 40 of the 90 clinically sensitive patients, but of these only 6 were positive, in each case to the specific fruit causing clinical symptoms. No intradermal tests were done.

MB sensitivity and asthma

After analysis of our data we became aware of an unsuspected relationship between the MB oral pruritus and asthma. Pollen or perennial bronchial asthma occurred in 70 of 90 (78 per cent) MB-sensitive patients. A control group of ragweed pollinosis patients with comparable skin tests showed asthma in 41 of 90 (47 per cent).

RESULTS OF IMMUNOLOGIC STUDIES

Agar gel diffusion

Clear precipitation lines were obtained between all antigens and their specific antisera, except for banana. In this case, no antibody was found despite the use of two rabbits and multiple injections of antigen by different routes. Either

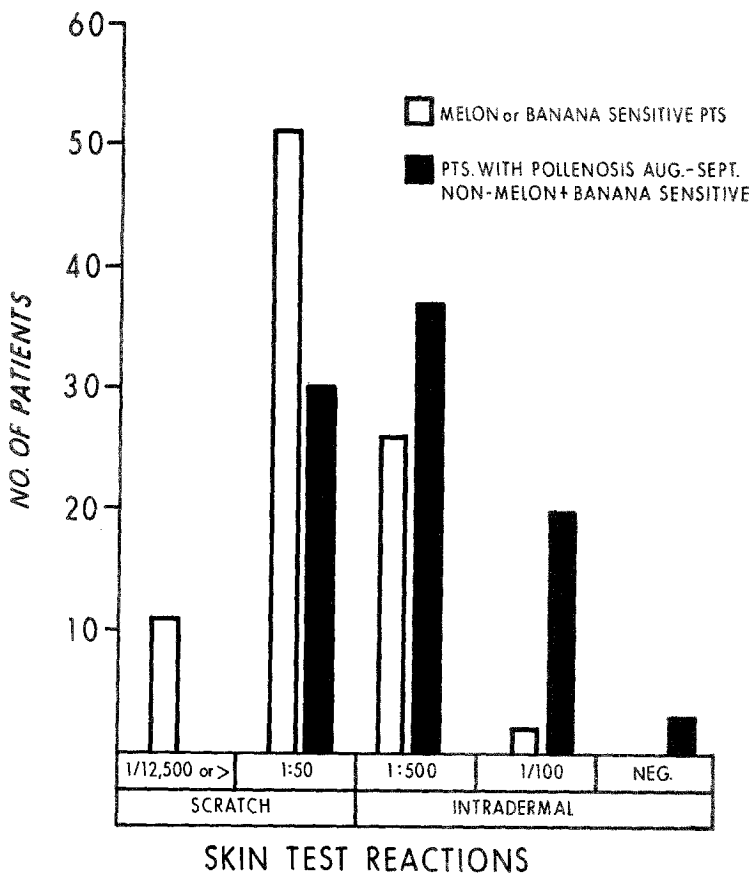


Fig. 2

Comparative ragweed skin test reactions between melon- and banana-sensitive patients and non-melon- and banana-sensitive patients.

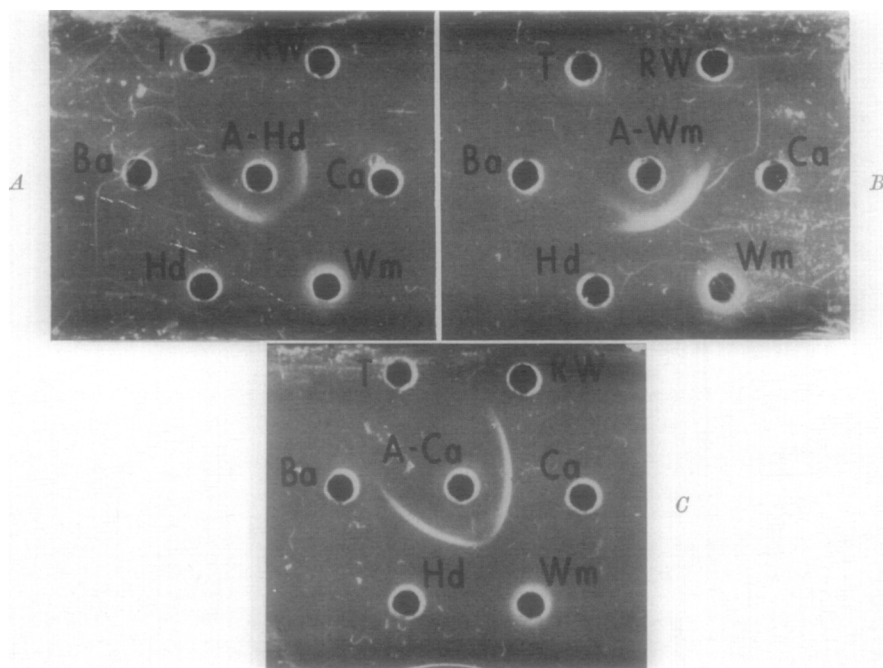
these two rabbits were not good antibody producers or banana extract in the concentration used is not a good antigen for the production of rabbit antibody.

A cross-precipitation line of identity was found between honeydew antibody and all three of the melons. (Fig. 3, *A*), indicating that these melons have at least one antigen in common. In addition, honeydew and cantaloupe share a common antigen that watermelon does not have (Fig. 3, *C*), and watermelon appears to have an antigen not present in the other two (Fig. 3, *B*).

As shown in Fig. 3 and Table III, no cross-precipitation occurred between ragweed and either melon or banana, or between timothy and melon or banana, or between melon and banana. Thus no common antigen, as demonstrated by agar gel diffusion, was found between ragweed or timothy and either melon or banana, although no measurable antibody to banana was produced in this study.

Passive cutaneous anaphylaxis

Strong cross-reactivity between ragweed antigen and all dilutions of anti-cantaloupe antibody was demonstrated by intense blue staining and edema of

**Fig. 3**

Ouchterlony gel diffusion. *A-Ca*, anti-cantaloupe antibody; *A-Wm*, anti-watermelon antibody; *A-Hd*, anti-honeydew antibody; *RW*, ragweed; *Ca*, cantaloupe; *Wm*, watermelon; *Hd*, honeydew; *Ba*, banana; *T*, timothy.

Table III. *Agar diffusion precipitation reactions*

Antibody	Antigens					
	Ragweed	Cantaloupe	Watermelon	Honeydew	Banana	Timothy
Anti-ragweed	+	0	0	0	0	0
Anti-cantaloupe	0	+	+	+	0	0
Anti-watermelon	0	+	+	+	0	0
Anti-honeydew	0	+	+	+	0	0
Anti-banana	0	0	0	0	0	0
Anti-timothy	0	0	0	0	0	+

Table IV. *Passive cutaneous anaphylaxis in guinea pigs*

Antibody (intradermal)	Antigens (intravenous)				
	Ragweed	Cantaloupe	Watermelon	Banana	Timothy
Anti-ragweed	+	0		0	
Anti-cantaloupe	+	+			
Anti-watermelon	0		+		
Anti-honeydew	0				0
Anti-banana	0			0	0
Anti-timothy	0		0	0	+

Specific challenges performed only where indicated with 0 or +.

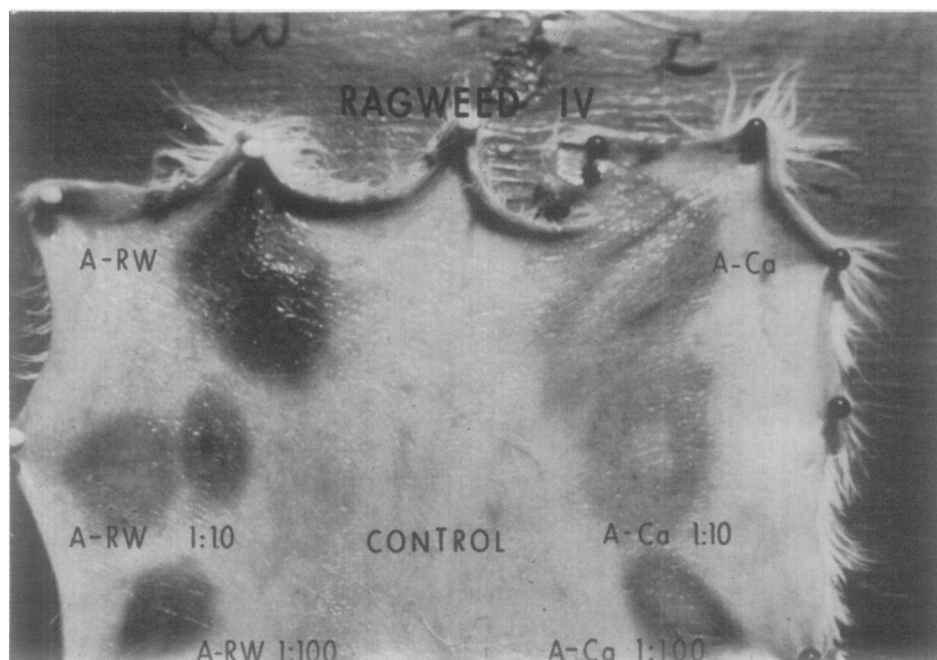


Fig. 4

Passive cutaneous anaphylaxis in guinea pig. *A-RW*: anti-ragweed antibody; *A-Ca*: anti-cantaloupe antibody. Ragweed antigen given intravenously following intradermal sensitization with antibody.

guinea pig skin in all three animals thus challenged. However, the converse of this situation, cantaloupe antigen versus anti-ragweed antibody, showed no cross-reactivity (Fig. 4, Table IV).

Strong specific reactions with edema and blue staining were obtained at all sensitized sites following intravenous challenge with the corresponding antigen except for banana, which further confirmed that we had not been successful in stimulating antibody production with this antigen. No cross-reactions were obtained with ragweed antigen against watermelon, honeydew, or banana antisera or with timothy antigen against watermelon or banana antisera. In each instance there was no reaction at the control site injected with nonspecific rabbit serum.

DISCUSSION

Clinically there appears to be a highly significant association between ragweed pollinosis and MB-induced oral pruritus. MB oral pruritus was not found in any of 620 non-pollinosis-allergic patients. This is quite remarkable, especially in view of the fact that several of this group were found to be highly sensitive to other foods. The demonstration of a common antigen between ragweed and cantaloupe gives a possible explanation for this phenomenon. While antigens stimulating antibody formation in the rabbit have never been proved identical with those causing human allergy, the occurrence of clinical symptoms induced by cantaloupe only in those patients with marked skin reactivity to ragweed is

suggestive of common antigenic determinants recognized by the human immunologic system.

Since the completion of our survey, two patients have been observed to have melon sensitivity and isolated grass pollinosis. Both had strongly positive scratch tests to grass, but each also had moderate intradermal reactions to ragweed. Since all of the MB-sensitive patients found during the survey showed varying degrees of skin test sensitivity to grass (in addition to ragweed), it is possible that grass pollen may also have a role in the syndrome. It would be interesting to know if MB oral pruritus occurs in association with grass pollinosis in Great Britain or other ragweed-free areas.

There is strong evidence of a banana-pollinosis relationship, but we were unable to obtain banana antibody in rabbits and could demonstrate no cross-reactivity between banana antigen and rabbit ragweed or timothy antibody. Banana oral pruritus was occasionally seen in patients allergic only to ragweed and frequently observed in patients whose primary clinical sensitivity was to ragweed. However, it was also seen in a few patients whose major pollen problem was grass. While our data suggest that ragweed is the significant pollen associated with banana sensitivity, further investigation is needed.

It is possible that pollinosis *per se* by virtue of its priming effect on oral mucosa in mouth-breathing hay fever patients might also explain this syndrome. Recent studies by Connell¹⁰ have shown that repeated doses of ragweed pollen on the nasal mucosa of ragweed-sensitive patients render them clinically sensitive to sorrel, whereas before the priming they were sensitive to sorrel only by skin test. However, many MB-sensitive patients note oral pruritus from melon or banana throughout the year, and one patient specifically challenged with cantaloupe in December reported an itching throat.

Pisani and associates³ report common antigens between multiple pollens and foods demonstrated by guinea pig passive cutaneous anaphylaxis. However, they specifically listed only those foods that had common antigens with grass, none of which were melon or banana, and did not test ragweed (the report is in an Argentinian journal). They advocate diet as one means of controlling pollinosis symptoms. We found no evidence that ingestion of melon or banana by sensitive patients aggravated pollinosis symptoms.

None of our 90 MB-sensitive patients had anaphylactic reactions which are often associated with a sensitivity to other foods, especially fish and nuts. Only one patient reported a mild swollen throat from melon, three noted hoarseness, three had wheezing, and seven had edema of the lips, the latter from banana. Most continued to eat the offending fruit with impunity since their symptoms were quite transient and were rarely accompanied by systemic manifestations. Pruritus was often quickly abolished by drinking water or taking an antihistaminic, and many have become completely tolerant.

In describing the itching sensation, patients invariably referred to the roof of the mouth, the pallet, or the throat, rarely mentioning the tongue. The tongue is as rich in mast cells as the other areas of the mouth⁸ but seems to react only in extreme sensitivities such as fish or nut anaphylaxis. Perhaps the lingual mucosa limits absorption.

The possibility that oral pruritus from banana ingestion might be caused by its serotonin content occurred to us but seems unlikely in view of the low incidence of pruritus from the injection of pineapple or tomato, both of which also contain comparable amounts of serotonin.

The absence of oral pruritus in children under the age of 8 is interesting but difficult to speculate about, since it may be due to lack of understanding rather than lack of symptoms.

The authors wish to acknowledge the help of Mr. John Wagner and thank him for his advice and technical assistance.

REFERENCES

1. Sheldon, J. M., Lovell, R. G., and Mathews, K. P.: A manual of clinical allergy, Philadelphia, 1967, W. B. Saunders Company, p. 198.
2. Scott, R. B., and Epps, R. P.: The treatment of nasal allergy, in Speer, F., editor: The allergic child, New York, 1963, Paul B. Hoeber, Inc., Medical Book Division of Harper & Row, Publishers.
3. Pisani, S., Duhau, A. M., Poiron, J. M., Poiron, M. P., Bocciolose, L.: Coincidental antigens between foods and pollens, *Sem. Med.*, Buenos Aires 113: 669, 1958.
4. Mallet, J. R.: Study of a case of respiratory pseudo-allergy to food from melon ingestion due to an allergy to "Candida albicans," *J. Med.*, Bordeaux 141: 719, 1964.
5. Snyder, R. D.: Allergic purpura, *Ann. Allerg.* 26: 328, 1968.
6. Strong, F. M.: Pressor amines in foods. Toxicity occurring naturally in foods, Publication No. 1354, Washington, 1966, National Academy of Sciences, National Research Council.
7. Bruce, D. W.: Serotonin in pineapples, *Nature* 188: 147, 1960.
8. Marshall, P. B.: Catechol amines in bananas, *J. Pharm. Pharmacol.* 10: 781, 1958.
9. Ovary, Z.: Immediate reactions in the skin of experimental animals provoked by antibody antigen interaction, *Prog. Allerg.* 5: 459, 1958.
10. Connell, J. T.: Quantitative intranasal pollen challenges. III. The priming effect in allergic rhinitis, *J. ALLERG.* 43: 33, 1969.
11. Selye, H.: The mast cell, London, 1965, Butterworth & Co., Ltd.