

Occupational asthma following inhalation of moth particles

Donald D. Stevenson, M.D., and Kenneth P. Mathews, M.D.,
Ann Arbor, Mich.

Because their larvae are desirable live fish bait, bee moths (Galleria mellonella; wax-worm) are raised in captivity. One of 18 persons, employed over a period of eight years at a commercial fish bait establishment, developed bronchial asthma resulting from heavy exposure to emanations of this moth. Skin tests, passive transfer, in vitro histamine release, and provocative bronchial inhalation tests indicated an immunologic mechanism to be responsible for the adverse effect. Extracts of other types of moths also elicited passive transfer reactions, as well as extracts prepared from different stages of the life cycle of Cecropia moths. In this particular case, however, extracts of several insects outside of the Lepidoptera order failed to produce positive passive transfer tests.

Among the many reported cases of allergic disease following inhalation of insect emanations,¹⁻¹¹ a few have been ascribed to members of the Lepidoptera order (moths and butterflies). Vaughan,¹² in 1928, apparently was the first to recognize the role of this latter order in producing asthma, and subsequent case reports in the following decade¹³⁻¹⁵ further suggested that moth emanations in certain specialized circumstances were etiologic in the production of asthma. However, these papers provided little evidence substantiating an immunologic basis for the reactions. The best documented case report on this subject was published in 1941 by Urbach and Gottlieb.¹⁶ These authors described asthma in a boy who was sensitive to clothes moths (*Tineola biselliella*), which were infesting the patient's home. He had positive skin test reactions to an extract of clothes moth, as well as to coddling moth. Negative skin test controls were observed on the parents. In addition, a crude bronchial challenge was effected by assigning the patient the task of grinding clothes moths with a mortar and pestle. Five minutes later, the boy developed an attack of bronchial asthma.

The purpose of this report is to describe an occupationally induced case of

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hypersensitivity to another genus of moth and to present special studies which demonstrate an immunologic basis for the reaction.

Case History

D. McK., a 22-year-old reliable white man, was first seen in June of 1965 for asthma of 2½ years' duration. The patient's family and childhood history were devoid of atopic disease. In the summer of 1962 (age 18), he began working for a bait company in southern Michigan. His major responsibility was raising and caring for moths (*Galleria mellonella*), the larval stage of which is used as fish bait. The moths were encouraged to complete their complicated metamorphosis under closed, artificial conditions and consequently thrived throughout the year. The patient spent much of his six-day work week confined in the moth domicile, which was heavily contaminated with dust, insect particles, and dead insect bodies. Three months after starting this job, he first developed rhinitis and asthma. The rhinitis gradually disappeared, but the asthma continued until the time he was first seen by us. The asthma was not confined to working hours but did tend to be more severe in the afternoon and evening of working days. Vacations were associated with partial improvement of symptoms. Asthma was slightly increased in the warm months but did not correlate with pollen seasons. Dusty houses, attics, and basements, other than his home and place of work, did not seem to increase asthmatic symptoms. Mold spores did not seem to be historically significant, except possibly for the increased summertime symptoms.

Because of increasing dyspnea and wheezing, failure of a standard bronchodilator treatment program, and realization that the bait shop was related to symptoms, the patient discontinued this employment in the summer of 1964. Since then he had been working full time as an inspector in an aluminum processing plant. During this time there had been gradual, but definite, improvement in his asthma. However, persistence of moderate symptoms prompted referral to our clinic in June of 1965. Additional history indicated that one visit to the bait shop in the preceding 10 months had been followed within several hours by a 6 hour attack of asthma. Two weeks prior to the initial evaluation in our allergy clinic, the patient moved from an old house to a new home without change in symptoms. The same overstuffed furniture, beds, rugs, etc. were used in both houses. Retrospectively, it was noted that the patient always wore his dirty working clothes home from the bait shop, up until his resignation in the summer of 1964.

Physical examination revealed a healthy appearing 6 foot 2 inch, 210 pound man. No abnormalities were noted except for generalized expiratory wheezes throughout both lung fields. The forced vital capacity was 4.5 L., FEV₁ was 3.2 L., and maximum expiratory flow rate was 275 L. per minute.

Chest roentgenogram, VDRL, urinalysis, and hematocrit were normal. Scratch and intracutaneous skin tests with animal danders, pollens, and individual molds were negative, but intracutaneous testing with house dust and a mold mixture produced small reactions. The patient returned one week later with dust samples obtained by vacuuming his own mattress, rugs, and stuffed furniture. After brief extraction in Coca's solution, scratch tests with these materials all gave 3+ reactions. Dust obtained from the aluminum factory was negative on testing. Ground adult insect, *Galleria mellonella*, in Coca's solution produced a 4+ reaction (scratch) with a negative control on the physician.

Before the authors saw the patient, he was started on hyposensitization to stock house dust and mixed mold extracts on a weekly basis. A follow-up visit in July of 1965 indicated that his asthmatic symptoms were decreasing, but physical examination still revealed expiratory wheezes. Forced vital capacity was 5.2 L., and FEV₁ was 4.2 L. with an MEFR of 500 L. per minute. A nasal smear revealed 10 per cent eosinophils. The patient returned in October of 1965 stating that his asthma had disappeared in the interim. Physical examination was negative. Forced vital capacity was 5.8 L., FEV₁ was 4.9 L., and MEFR was 600 L. per minute. Results of intracutaneous skin tests on the patient with extracts, to be described in a later section, are given in Table I. Further special studies will be described. The patient has remained entirely asymptomatic to the time of submission of this paper. A visit to the bait shop revealed that the owner, who has been in the "moth larva" business for 8 years, has never

Table I

<i>Extract</i>	<i>W/V</i>	<i>Wheal (mm.)</i>	<i>Erythema (mm.)</i>	<i>Graded reaction</i>
Galleria wings	1:100,000,000	12+	25	4+
Cecropia moth	1:50,000	pseudopods 9	20	3+
May fly	1:10,000	3	0	—
Silk	1:50	3	0	—

had respiratory tract symptoms. A total of 18 employees have worked there during the 8 years, with known allergic symptoms appearing only in our patient. The owner and one of his current employees were skin tested intracutaneously with Galleria extract, 1:1,000,000, and both were negative.

EXPERIMENTAL DATA

Preparation of extracts

Adult bee moths (*Galleria mellonella*) were obtained from the bait shop. Representatives from all stages of the metamorphosis of Cecropia moths were obtained from the University of Michigan Zoology Department.* The insects were frozen alive or shortly after dissection and stored at -20° C. They were broken up into smaller sections with scissors. Defatting in a soxhlet apparatus was continued until the returning ether was approximately clear (slightly yellow tinged). Moth parts were then ground with a mortar and pestle, weighed, and extracted in phosphate buffered saline, pH 8.0, for 48 hours at about 4° C. The extracts were centrifuged at 1,600 g for 30 minutes at 4° C., and the supernatants were recentrifuged in the same manner. After passage through a 1.2 micron clarifying filter, sterilization was achieved by passage through a Millipore filter. Galleria and Cecropia extracts were prepared without phenol or other preservatives. The total nitrogen (TN) and phosphotungstic acid precipitable nitrogen (PTA-N)¹⁷ content of the extracts, as measured by the micro-Kjeldahl method, were as follows: Galleria mixture† 1:10 (W/V) contained 788.8 μ g PTA-N per milliliter (78,880, PNU per milliliter) and 4,732.8 μ g TN per milliliter. Cecropia wing 1:50 (W/V) contained 43.38 μ g PTA-N per milliliter (4,338 PNU per milliliter) and 201.38 μ g TN per milliliter. In addition, representatives from other insect orders were obtained from Hollister-Stier (mayfly, caddis fly, mosquito, Hymenoptera mixture, and deerfly). Extracts of silk moth, noctuid moth, and wax moth‡ supplied by Dr. Frank Perlman had been prepared as described in his publication.¹⁸

Special tests

Passive transfer or Prausnitz-Küstner (P-K) tests. Tenfold serial dilutions of insect extracts were prepared with phosphate buffered saline, pH 7.0, until

*Through the courtesy of Dr. David G. Shappirio.

†This mixture consisted of wings, bodies, and emanations.

‡Wax moth used by Dr. Perlman was the same insect as our Galleria. To avoid confusion, Dr. Perlman's extract will be referred to as wax moth and ours referred to as Galleria.

Table II. Results of P-K tests. The sites had been sensitized 24 hours previously by 0.1 ml. quantities of the patient's serum and challenged with 0.02 ml. of the indicated allergen dilutions injected intracutaneously

Testing	Extract dilution (W/V)	P-K recipient No. 1			P-K recipient No. 2		
		Wheal (mm.)	Ery- thema (mm.)	Graded reaction	Wheal (mm.)	Ery- thema (mm.)	Graded reaction
Sept. 18, 1965							
Diluent con- trol		4	0	—	4	0	—
Galleria mix- ture	1:1,000,000	6	27	2+	5	25	2+
Galleria wings	1:1,000,000	5	27	2+	6	32	2+
Galleria wings	1:100,000				11	38	3+
Cecropia wings	1:500,000	5	24	2+	6	20	1+
Cecropia body	1:500,000	4	11	±	4	21	1+
Cecropia pupa	1:100,000	6	30	2+	8	32	2+
Cecropia larva	1:500,00	6	28	2+	5	31	2+
Mayfly	1:100,000	5	0	—	6	21	2+*
Mayfly	1:10,000	3	0	—	10	26	2+*
Mosquito	1:100,000	4	0	—	3	0	—
Mosquito	1:10,000	2	0	—	4	?	±
Hymenop- ter mixture	1:100,000	4	0	—	4	0	—
Hymenop- ter mixture	1:10,000	3	0	—	4	0	—
Deerfly	1:10,000				4	0	—
Caddis fly	1:500	3	0	—			
April 8, 1966							
Diluent con- trol		6	0	—			
Galleria wings	1:100,000	7	47	2+			
Wax moth†	1:25,000	12	55	3+			
Wax moth†	1:2,500	15	57	4+			
		Pseudo					
Noctuid moth†	1:50,000	7	27	2+			
Noctuid moth†	1:5,000	10	45	3+			
Silk worm moth†	1:30,000	10	32	3+			
Silk worm moth†	1:3,000	9	35	3+			

*P-K recipient No. 2 also had 2+ reactions to 1:100,000 and 1:10,000 mayfly allergen at control test sites not sensitized with the patient's serum. Otherwise, the control tests with all other antigens on both recipients were negative.

†Provided by Dr. Frank Perlman.

intracutaneous skin tests on the nonsensitized skin of 2 potential passive transfer recipients were unequivocally negative when compared with diluent control sites. All P-K testing was carried out in September of 1965 and January and April of 1966, with aliquots of the patient's serum stored at about -20° C. and extracts stored at about 4° C. There seemed to be no diminution in reactivity during this period. P-K testing was performed on two recipients in the usual manner.¹⁹ Results are presented in Table II. Additional observations showed that 1:5 and 1:25 dilutions of the D. McK. serum gave a passive transfer reaction when challenged with 1:100,000 *Galleria* wing extract, while results were negative with 1:125 serum dilution. When the P-K sites, which had failed to react with Caddis fly, were subsequently challenged with *Galleria* 1:100,000 and waxworm 1:25,000, significant reactions were observed.

In vitro histamine release tests. *Galleria* wing extract was added to 3 ml. aliquots of the patient's whole blood, and histamine was measured in the supernatant plasma after 30 minutes incubation at 37° C. by a modification of the spectrofluorometric method of Shore, Burkhalter, and Cohen.²⁰ Preliminary tests with normal blood indicated that 0.1 ml. of tenfold dilutions of *Galleria* wing extract higher than 1:1,000 did not produce nonspecific histamine release, but 0.1 ml. of 1:1,000,000 extract yielded a 70 per cent release of histamine from its bound form in D. McK.'s leukocytes.^{21, 22}

Gel diffusion and immunoelectrophoresis. The patient's serum was diffused against varying concentrations of *Galleria* wing extract in Ouchterlony plates. Immunoelectrophoresis was carried out by the micro method of Scheidegger.²³ *Galleria* mixture extract 1:10 was electrophoresed in the gel at pH 8.2, and D. McK.'s serum was added to the longitudinal troughs. As expected in atopic-type hypersensitivity, no precipitin bands were visible after staining either type of preparation.

Provocative bronchial inhalation challenge. This test was performed in October, 1965, when the patient was clinically asymptomatic and receiving no medications. The test extracts were placed in a DeVilbiss No. 40 nebulizer connected through a Y tube to a compressed air source. By occlusion of the open end of the Y tube during inspirations, 1 ml. of solution was delivered to the patient in about 3 minutes. The physician's auscultatory findings and the patient's subjective appraisal of asthmatic symptoms were noted each time triplicate tracings were made of the patient's maximal expiratory effort, with a Pulmonor Spirometer recording at a speed of one inch per second. The above studies were obtained before challenge, immediately afterward, and every 5 minutes for the next 15 minutes. Immediately thereafter the next challenging inhalation was administered. The patient was conscientious, and the tracings were felt to represent maximal effort. From them, the forced vital capacity, FEV₁, and the MEF₅₀ were measured. The patient was first challenged with the buffered saline diluent. He knew that he would eventually receive *Galleria* extract, but he was unaware when this would be. Three adults who had experienced recent asthma and had negative skin test reactions to *Galleria* extract served as controls and were challenged with the same 1:100,000 *Galleria* extract which produced definite airway obstruction and asthmatic signs and symptoms

Table III. Bronchial inhalation challenge, Oct. 28, 1965

Extract	Time of observation*	Mean forced vital capacity (L.)	Mean FEV ₁ (L.)	Mean MFE (L./minute)	Clinical evaluation
—	Before	5.65 (5.6-5.7) †	4.3 (4.2-4.6) †	480 (450-500) †	Normal
Phosphate buffered saline	Immediately afterwards	5.6†	4.4†	760 (500-900)	Normal
	5 minutes	5.6 (5.5-5.7)	4.6†	900†	Normal
	10 minutes	5.7 (5.6-5.8)	4.7 (4.6-4.8)	870 (700-1,000)	Normal
	15 minutes	5.7†	4.8†	1,000†	Normal
Galleria wing extract, 1:100 million	Immediately	5.67 (5.6-5.7)	4.8†	930 (900-1,000)	Normal
	5 minutes	5.63 (5.6-5.7)	4.63 (4.5-4.7)	870 (700-1,000)	Normal
	10 minutes	5.75†	4.8†	1,000†	Normal
	15 minutes	5.76 (5.7-5.9)	4.83 (4.7-5.0)	1,030 (900-1,200)	Normal
Galleria wing extract, 1:10 million	Immediately	5.71 (5.65-5.8)	4.53 (4.5-4.6)	800 (500-1,000)	Normal
	5 minutes	5.7†	4.63 (4.6-4.7)	900 (500-1,200)	Normal
	10 minutes	5.6†	4.53 (4.4-4.6)	930 (800-1,000)	Normal
	15 minutes	5.63 (5.5-5.7)	4.6 (4.5-4.7)	830 (500-1,000)	Normal
Galleria wing extract, 1:1 million	Immediately	5.5 (5.4-5.7)	4.15 (4.0-4.4)	730 (600-1,000)	Normal
	5 minutes	5.57 (5.5-5.6)	4.2 (4.0-4.3)	550 (300-900)	Normal
	10 minutes	5.5 (5.4-5.6)	4.37 (4.3-4.5)	870 (800-900)	Normal
	15 minutes	5.5†	4.27 (4.2-4.4)	470 (300-800)	Normal
Galleria wing extract, 1:100,000	Immediately	5.0 (4.9-5.1)	3.57 (3.4-3.7)	370 (350-400)	Patient dyspneic, lungs clear
	5 minutes	5.17 (5.0-5.3)	3.57 (3.5-3.7)	400 (350-500)	Expiratory wheezes
	10 minutes	4.8 (4.7-4.9)	2.9 (2.8-3.0)	250 (200-300)	Expiratory and inspiratory wheezes
	13 minutes	4.9 (4.6-5.1)	3.13 (3.0-3.2)	250†	Expiratory and inspiratory wheezes
	16 minutes	5.03 (4.9-5.1)	3.26 (3.0-3.4)	400 (300-600)	Expiratory and inspiratory wheezes
	18 minutes	4.87 (4.8-4.9)	3.26 (3.0-3.4)	370 (300-400)	Continued wheezes, less dyspnea
	20 minutes	5.33 (5.3-5.4)	3.73 (3.6-3.9)	530 (500-600)	Expiratory wheezes only
	24 minutes	5.47 (5.4-5.5)	3.83 (3.8-3.9)	730 (700-800)	Expiratory wheezes only
	32 minutes	5.63 (5.6-5.7)	4.06 (4.0-4.2)	800 (500-1,000)	Lungs clear, patient tired

*Time measurements were made before or after nebulization.

†Range of triplicate determinations.

‡All 3 triplicate determinations the same as mean.

in the patient. None of the control subjects developed measurable bronchospasm or symptoms following inhalation of *Galleria* extract. These control challenges seemed reasonably to exclude the possibility that the extract was functioning as an irritant rather than as an antigen. Results of the tests on the patient are shown in Table III. Inspection of the data shows a marked difference in pulmonary function values before and after challenge with 1:100,000 *Galleria* wing extract, and paired t test analysis of the V.C., FEV₁, and MEFR values shows the differences to be significant at the 5 per cent level of confidence or less.

DISCUSSION

The clinical history obviously implicated *Galleria mellonella* emanations as being responsible for much of the patient's reported asthma, and the skin tests, passive transfer, and histamine release data strongly support the hypothesis that an immunologic mechanism is involved. However, in view of the frequent occurrence of skin test and passive transfer reactions to various insect allergens upon routine testing of allergic patients,^{24, 25} the possibility that the skin test reactions were coincidental was considered. Hence, 50 allergic outpatients were skin tested with *Galleria* mixture extract (1:1,000) and noctuid moth extract (1:500). Twenty-six responded with significant wheal-and-flare reactions to at least one of these concentrated moth extracts. In addition, 4 of 7 normal subjects gave immediate-type intracutaneous reactions to *Galleria* wing extract (1:10,000) and/or to wax moth extract (1:2,500). One of the 7 reacted to the 1:1 million concentration of *Galleria* wing extract which had produced the positive immediate-type reaction in the patient's skin. These observations led to the performance of the provocative inhalation challenge tests. The fact that the patient's respiratory tract responded to a high dilution of *Galleria* antigen supports the assumption that this material is capable of causing obstructive airway disease in this case. The finding that other patients with recent bronchial asthma failed to react to the same concentration of moth allergen strongly suggests that the patient's response was due to immediate-type hypersensitivity rather than to an irritant effect.

It is noteworthy that other cases of inhalant insect allergy have resulted from heavy occupational exposures; for example, mushroom fly allergy in persons employed in growing mushrooms,⁷ beetle allergy in a museum curator,⁴ or moth allergy in an entomologist.¹³ In our case the patient was exposed to emanations from the bee moth (*Galleria mellonella*), also known as the wax moth or wax worm. This common beehive inhabitant and pest is found throughout Europe and the North American continent with increased concentration near apiaries. The eggs are laid near or in the honeycomb and hatch into larvae which burrow through the honeycomb, feeding upon and destroying the comb. Pupation occurs in thick, tough, bee-proof cocoons. The evolution of a crysalis and transformation into an adult moth (Fig. 1) complete metamorphosis. In nature, there are three broods per year.²⁶ Some commercial bait shops have raised and stimulated this moth species in captivity to produce many broods per year. In addition, metamorphosis can be stopped at the larval stage and the larvae held in storage until seasonal fishing demands provide a market for their sale. The closed rooms in

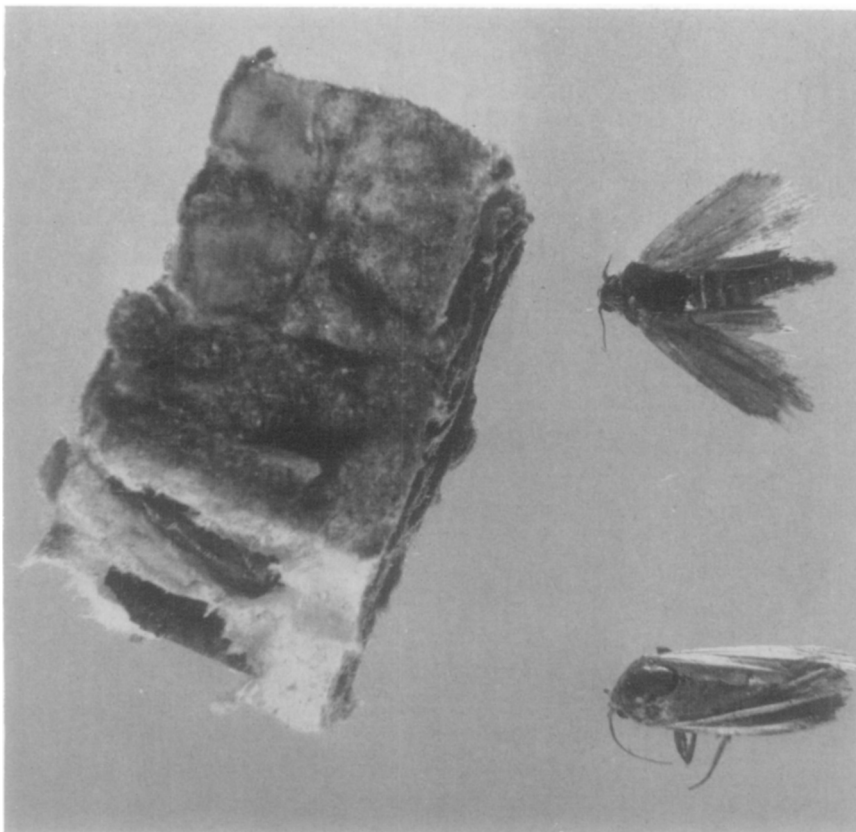


Fig. 1

Adult *Galleria* moths are shown at the right. Corrugated paper at the left has been torn in order to expose larval forms.

which the adult female moths lay their eggs are filled with insect parts and "dust." Employment in this rather unique environment provided the setting whereby our patient was exposed to a high concentration of airborne moth particles on a prolonged, daily basis. It is noteworthy, however, that D.McK. was the only one of 18 employees to develop clinical hypersensitivity to *Galleria* emanations under these conditions of intense exposure.

In addition to reacting with *Galleria* antigens, the patient's serum gave positive passive transfer test reactions with extracts of *Cecropia*, noctuid moth, and silk moth at high dilutions of allergen. It seems most likely that these results are due to cross-reaction antigens within the order *Lepidoptera*. Using skin and passive transfer tests, Perlman²⁷ has reported that cross-reactions within insect orders are frequent and that cross-reactions outside the order are not uncommon. Langlois, Shulman, and Arbesman²⁸ have reacted rabbit anticaddis fly sera against a variety of insect extracts in double gel diffusion and demonstrated multiple cross-reacting lines of precipitation. The relationship of these precipitating antigens to human allergens is uncertain, but such studies do indicate the ex-

istence of common antigens in a number of both closely and distantly related insects. Unfortunately, the antigenic complexity of insects and the enormous number of species are so overwhelming that systematic, comparative immunologic studies have not been pursued in any depth. Although the existence of cross-reacting antigens between different orders of insects seems established, it is interesting that the serum of our patient failed to react with extracts of several insects outside the Lepidoptera order. It also is noteworthy that the serum did react with extracts prepared from different stages of the life cycle of *Cecropia* moths.

An incidental finding was the frequent occurrence of delayed, erythematous, indurated skin lesions at the site of intracutaneous injections of Lepidoptera extracts. Five out of 7 normal individuals exhibited reactions at 24 hours to relatively concentrated (1:2,500) wax moth extract, and 2 of 7 reacted in this manner to concentrated (1:10,000) *Galleria* wing extract. These responses did not correlate with the previously mentioned immediate skin reactions to these concentrated extracts, and in one individual delayed reactions could be elicited with a high dilution (1:1,000,000) of *Galleria* wing extract, which did not elicit immediate-type reactions in anyone except the patient and one normal person. These data are insufficient to determine with certainty whether irritant effects or delayed hypersensitivity are responsible for these delayed skin test reactions. The latter possibility merits consideration in view of a report²⁹ that a group of seamen developed contact dermatitis from sleeping in sheets contaminated with crushed moth bodies. Thirty-one out of the 45 crewmen developed the dermatitis 6 to 24 hours after exposure, and delayed skin test reactions with moth extracts were positive in those afflicted with the dermatitis. The high incidence of this delayed-type reaction in an otherwise normal population contrasts strikingly with the highly selective immediate-type hypersensitivity demonstrated by the patient reported in this paper.

Finally, there was the question as to whether the spontaneous symptoms in this case were due entirely to *Galleria* allergy. Although improved, the patient's symptoms did not disappear completely after terminating his employment at the bait shop. He also gave slight intracutaneous test reactions to a mixed fungus and one house dust extract, but our experience with these particular extracts has indicated that they apparently contain small amounts of irritants capable of producing small nonspecific reactions. On the other hand, it is noteworthy that the patient customarily wore his work clothes home from the bait shop, and extracts of his own house dust produced pronounced scratch test reactions whereas stock house dust extracts yielded negative skin tests by the scratch technique. The history also did not indicate difficulty on exposure to ordinary house dust. Furthermore, his complete clearing of symptoms in the late summer of 1965 followed moving in June to another house where contamination with *Galleria* allergen through the household effects might well have become dissipated over a period of time. Thus, we believe that the moth allergen(s) caused all of the difficulty, but this interpretation is open to question because, unfortunately, hyposensitization with mixed fungus and the house dust extracts had been instituted by another physician shortly before we first saw the patient.

Addendum

Since submitting this manuscript for publication, the patient was seen again in November, 1966. He continues to be entirely asymptomatic but has understandably avoided further visits to the bait shop. Physical examination and pulmonary function studies were again normal.

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