

ALLERGY TO CADDIS FLY (TRICHOPTERA)

II. CLINICAL ASPECTS

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THE caddis fly (*Trichoptera*) has been recognized as an excitant of allergic respiratory symptoms for nearly thirty years. Since no reports on caddis fly allergy have appeared in the literature for many years, a résumé of my clinical experience with this type on the Niagara frontier has seemed opportune.

The head of the Niagara River as it emerges from Lake Erie is heavily infested by these flies. Because of the location on either side of the river of two cities—Fort Erie, Canada (population 9,200) and Buffalo, New York (population 600,000), a large human population has been exposed to their emanations. The residential section of Fort Erie extends to the water's edge and the principal larval beds of the flies lie on the river bottom along the Fort Erie front. As a result, exposure to the flies in Fort Erie has been much greater than in Buffalo.

THE INSECT

The *Trichoptera* are aquatic insects which live in fresh water, except in the adult (reproductive) stage. The wings of the adult are covered with microscopic hairs (setae) which are very easily dislodged. These hairs, and to a less extent the dried particles of their dead bodies, are airborne and, by inhalation, induce the allergic symptoms. They are not biting insects.

Along the Niagara River, the adult flies appear about mid-June and persist until the end of September, the contiguous land being more or less continuously infested for a distance inland of several hundred yards. At irregular intervals during their season, usually in the late afternoon and evening, the insects may form great swarms extending a mile or two along the banks and inland up to one-half mile. Such swarms may contain many millions of individual flies and may persist for several days.

For a detailed discussion of the classification, distribution, and habits of the *Trichoptera*, I would refer to my earlier article¹ which appeared in the March, 1957, issue of THE JOURNAL OF ALLERGY.

THE CADDIS-FLY-SENSITIVE PATIENT

The emanations (setae and body particles) of the caddis fly are intrinsically innocuous; normal persons are not affected by them, even on heavy exposure. Persons allergic to these insects exhibit all the symptoms that are characteristic of respiratory allergy: nasal, conjunctival, and bronchial. I have seen no case of atopic or contact dermatitis in which sensitivity to the caddis fly appeared to be causally related.

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Of the fifty-seven patients considered below, in whom treatment with caddis fly extract seemed indicated, thirty were males and twenty-seven were females. The youngest was 6 years old and the oldest was 57 years old when they first came under my observation. There were seven children 10 years of age or younger, fourteen persons between the ages of 11 and 20 years, ten between the ages of 21 and 30 years, eighteen between the ages of 31 and 40 years, six between 41 and 50 years, and two over 50 years. All were white.

The following description is a synthetic picture based on the patients in my experience who were unequivocally allergic to caddis fly and in whom this fly was the primary excitant of their symptoms.

The patient has experienced fairly marked exposure to the caddis fly for several years, some as much as thirty years, before the symptoms first appear. The early symptoms may be typical vasomotor rhinitis, mild asthma, or both. As the succeeding seasons recur, the symptoms increase in intensity; conjunctival itching and redness are more pronounced than in pollinosis; nasal obstruction is very troublesome. Asthma is a more frequent symptom than in pollinosis, and is often severe. These symptoms appear about mid-June and become marked by the end of June in the Niagara area, when the first dense swarms of the flies occur. During the rest of the summer the symptoms persist, at least in mild degree, with exacerbations coincident with fluctuations in the concentration of the flying insects, and are marked during the periods of the swarms. As the concentration of the flies decreases during September, the symptoms ameliorate and usually cease by the end of September. During the season, the patient can secure marked, and often complete, relief of symptoms by going inland five or six miles from the river. Several patients have arranged to sleep thus far away during the heavy swarms. A number of patients who have moved to a place of residence six to eight miles or more away from the river have discontinued treatment entirely.

From the end of September until the following June, the patient is symptom free. However, it has often happened that a patient has entered an attic or a boathouse during the interval between the caddis fly seasons and has developed typical symptoms when he has stirred up the dead flies lying there, as the insects find their way through any house opening during the summer swarms.

Adequate hyposensitizing treatment has resulted in good control of the symptoms,^{4, 5} particularly of the asthma. Most treated patients still experience some nasal and eye symptoms during the season when the flies are thick, if they remain in the areas of heavy infestation, but can control these symptoms with antihistaminics.

One case, unique in my experience, is that of a 12-year-old boy who had mild perennial vasomotor rhinitis, but who developed repeated corneal ulcers only during the caddis fly season. He showed a very marked skin reaction to caddis fly, a slight reaction to feathers, and negative reactions to pollens, May fly, molds, inhalants, and foods. Perennial hyposensitizing injections relieved the corneal ulcers.

ATOPIC CHARACTERISTICS

As Parlato^{2, 3, 5} and I^{4, 6} have shown, direct skin tests with an extract of the whole fly yield immediate, wheal type reactions in persons allergic to the caddis fly. Specific reagins to caddis fly are demonstrable in the patient's blood serum by the Prausnitz-Küstner method.^{2-4, 7} Positive conjunctival tests are obtained with both the wing hairs and body particles, as well as with the extract.²⁻⁴ Typical symptoms can be induced by the deliberate inhalation of the hairs and body particles.²⁻⁴

Some years ago I succeeded in inducing nonfatal anaphylactic symptoms in a small number of guinea pigs, using caddis fly extract for the sensitizing and shocking doses. The study was not completed, but apparently a large dose of the antigen is required to produce high sensitization.

The antigen in the extract of the whole fly appears to be multiple, since extracts from separate species of caddis fly have been shown to contain both common factors and differing factors.⁶

COLLECTION OF THE INSECTS AND PREPARATION OF THE EXTRACT

The caddis flies may be secured in quantity by means of a large trap, lighted inside with all but the mouth shaded and set at dusk adjacent to the water's edge. They also may be caught alive with a wide-mouth (24 inch) conical net made of cotton mosquito netting. By repeated air sweeps, as the flies swarm over bushes in daylight or around outdoor lights in the evening, the insects accumulate at the tip of the cone and are killed by inserting the tip into a wide-mouth jar containing carbon tetrachloride. In my experience, the net method has yielded a supply somewhat less contaminated with other insects than the trap. Supplies of dead caddis flies swept up from surfaces beneath outdoor lights have usually been so contaminated with other insects and dirt as to be nearly worthless. Whatever the method of securing them, the catch is usually a mixture of several species of caddis fly.

After collection, the flies are spread out thinly on a clean surface for two or three days to dry. They are then carefully sorted to remove extraneous insects (moths, beetles, May flies, flying ants, etc.), and in addition may be sifted to remove gnats, mosquitoes, and midges. The whole flies are defatted (an astonishing amount of fatty material is removed), and extracted in Coca's solution. The extract is sterilized by Seitz filtration, tested for sterility, and stored at refrigerator temperature.

Standardization has been done on the protein nitrogen basis (phosphotungstic-acid-precipitable nitrogen method of Cooke and Stull¹²). The initial extract is made up on a 10 per cent basis: 10 grams of dried defatted flies to 100 c.c. of extracting fluid. The protein nitrogen content of this extract has averaged about 0.30 mg. per cubic centimeter.

If the defatted flies are to be preserved in the dry state for future extraction, they should be protected from moisture by an efficient desiccating method which will also prevent moldiness, to which they are prone. They should be kept in a refrigerator.

SKIN TEST TECHNIQUE

Skin testing has been done by the intradermal method, using dilutions of the extract containing 10 units, 100 units, and 1,000 units of protein nitrogen per cubic centimeter. These strengths correspond, roughly, to 1:30,000, 1:3,000, and 1:300 dilutions, respectively, on the weight-to-volume basis. The extract is not intrinsically irritating when used in appropriate dilutions.

In addition to the caddis fly, patients whose allergic symptoms were limited to the summer months have been routinely tested with pollens, four mold spores (*alternaria*, *aspergillus*, *hormodendron*, *penicillium*), and frequently May fly. Patients with perennial symptoms have also been tested with the usual inhalants and common foods.

CLINICAL MATERIAL

The material for this report is based on the case records of 623 private allergic patients whom I have skin tested with caddis fly extract since 1940. Patients tested prior to that date have been excluded, since their full records are no longer available.

These 623 patients represent, to some extent, a selected group, because I have tested with caddis fly those patients in whom some exposure to the insects has seemed to me a possibility; on the other hand, I have *not* always tested with caddis fly the many patients in whom such exposure seemed improbable or nonexistent.

RESULTS OF SKIN TESTS

Of the 623 patients, 236 gave no skin reaction to caddis fly and 172 gave a slight reaction only to the strongest test dilution. A moderate reaction to the strongest test dilution was obtained in 141 patients and a marked reaction was obtained in seventy-four patients. Thus, 215 patients showed definite skin sensitivity to the flies and 408 showed negative or indeterminate reactions (Table I).

TABLE I. RESULTS OF INTRADERMAL TESTS WITH CADDIS FLY

REACTION	NUMBER OF PATIENTS	PER CENT
Negative	236	37.9
Slight only	172	27.6
Moderate only	141	22.6
Marked or greater	74	11.9
	623	100.0

The incidence of definitely positive skin tests (moderate and marked) of patients living in the immediate vicinity of the Niagara River and of others living twenty miles or more distant appears in Table II. These figures show a definite decrease in the occurrence of stronger skin test reactions with the increase in distance of residence from the known area of concentration of the flies.

TABLE II. RELATIONSHIP BETWEEN PLACE OF RESIDENCE AND INCIDENCE OF DEFINITELY POSITIVE SKIN TESTS TO CADDIS FLY

RESIDENCE	NO. OF PATIENTS TESTED	PATIENTS WITH MODERATE OR MARKED TESTS	PER CENT
Fort Erie; heavy exposure	37	22	60
Buffalo and on Niagara River within 10 miles of larval beds; moderate to light exposure	279	99	35
Inland more than 20 miles from larval beds, and not on other large streams or lakes; little or no exposure	142	31	22

As would be expected in allergic persons, no patient has been observed who gave a positive skin test solely to caddis fly. All have reacted weakly or strongly to a few, to several, or to many of the other allergens included in the series of tests applied.

The interpretation of a definitely positive (moderate or marked) skin test to caddis fly in a given patient presents the same problems as in the case of any pollen or other inhalant allergen. Since the caddis fly extract is not intrinsically irritating in the dilutions used, we must assume that, to develop this skin sensitivity, such a patient has been exposed at some time to caddis fly or to some other insect which is related antigenically to the caddis fly.

TREATMENT

The circumstances of history, seasonal symptoms, and exposure to the insects made advisable the treatment by hyposensitization of fifty-seven patients out of 387 patients who yielded a positive skin test (slight or greater) to caddis fly. Of these fifty-seven patients, twenty-four resided in Fort Erie where the exposure is heavy and ten resided in Buffalo. The remaining twenty-three patients resided in an area within twenty miles of the head of the Niagara River and were exposed by their not infrequent trips into the infested area.* These patients have been grouped in Table III according to the relative importance of the caddis fly in the production of their symptoms.

TABLE III. CADDIS FLY FACTOR IN PRODUCTION OF SYMPTOMS IN TREATED PATIENTS

GROUP	IMPORTANCE OF CADDIS FLY FACTOR	NUMBER OF PATIENTS
A	Caddis fly primary	6
B	Caddis fly a major factor	4
C	Caddis fly, pollens, etc., about equal	10
D	Caddis fly minor	37

No patients have been observed in whom the caddis fly was the sole excitant of their symptoms, and therefore there are none in whom treatment with caddis fly extract alone appeared justified. In addition to caddis fly,

*A questionnaire addressed to the leading allergists in Buffalo in November, 1956, disclosed that they had sixty-three patients currently under hyposensitization with caddis fly. With my own current patients, there were eighty-four patients under treatment at that time in our area.

fifty patients were treated with one or more pollens, thirty-two with one or more molds, nineteen with May fly, and forty-four with house dust or other inhalants.

The initial dose of the caddis fly extract has been 2 to 10 protein nitrogen units. The maximum dose reached has been between 500 and 10,000 units, and this dose has been continued every four weeks on a perennial basis. The duration of treatment in each patient has ranged from nine months to over seventeen years. Nine patients have been treated for over twelve years. Excluding eleven patients who received treatment for less than two years, there are forty-six patients whose treatment period has averaged a little over seven years. Twenty-one patients are still under treatment, with the duration of treatment ranging from one and one-half years to over seventeen years and an average period of just over six years.

The incidence of local and constitutional reactions attributable to the caddis fly extract has been about the same as in pollen treatment. Both have occasionally been marked, although I have met with no dangerous general reactions.

The results of treatment in these fifty-seven patients are shown in Table IV.

The effectiveness of hyposensitization with caddis fly extract can be judged, I believe, only in the ten patients in Groups A and B, as the picture becomes complicated by allergy to other substances in Groups C and D, and the results could be attributed largely to the treatment with the other extracts used. These ten patients (nine from Fort Erie and one from Buffalo) all resided within a few hundred yards of the river's edge.

TABLE IV. RESULTS OF TREATMENT WITH CADDIS FLY

GROUP	NUMBER OF PATIENTS			TOTAL
	GOOD	FAIR	POOR	
A	4	1	1	6
B	2	2	0	4
C	9	1	0	10
D	21	10	6	37

The one patient in Group A who yielded a poor result was very sensitive to caddis fly, by which he was surrounded during his working hours as a Canadian inspector at the Peace Bridge. He gave strong skin reactions to caddis fly and to house dust, but negative skin reactions to all the pollens and other inhalants and only mild reactions to one mold and to May fly. The dust was included in his injections with caddis fly. He could secure practically complete relief of symptoms during the caddis fly season by going five or six miles inland. After twenty months of perennial injections, with poor protection from the caddis flies at his work, he was transferred to another area free of these flies.

POSSIBLE ANTIGENIC RELATIONSHIP BETWEEN CADDIS FLY AND OTHER ALLERGENIC INSECTS

The diagnosis and treatment of allergy to the caddis fly present no particular problems in patients skin positive to these flies who reside or vacation in areas where the flies are abundant. In the combination of typical symptoms

coinciding with the caddis fly season, a positive skin test, and demonstrable exposure to the flies, one will have reasonably secure grounds on which to base the diagnosis and the decision as to specific treatment.

A more difficult situation is that met with in the patient who is skin positive to caddis flies but who is not, so far as is known, exposed to any concentration of them. This situation requires some discussion.

Pertinent to this problem is allergic sensitivity to May fly (*Ephemerida*), which Figley⁹ reported in 1929, and to butterflies and moths (*Lepidoptera*), reported by Parlato^{7, 8} in 1932 and by Urbach and Gottlieb¹⁰ in 1941.

In my group of 623 cases, 196 patients yielding moderate or marked reactions to caddis fly were also tested with May fly extract in comparable dilutions (Table V). The May fly occurs to some extent in the immediate Niagara area, and is abundant along the sandy shores of Lake Erie three or four miles distant, so that exposure to this insect is probably common among the population of the region.

TABLE V. COMPARABLE SKIN REACTIONS TO MAY FLY IN 196 PATIENTS SKIN POSITIVE TO CADDIS FLY

COMPARATIVE SKIN REACTIONS TO CADDIS FLY AND MAY FLY	PER CENT
Caddis fly test the stronger	43
Caddis fly and May fly test about equal	32
May fly test the stronger	17
May fly test negative	8

The caddis fly is distributed over all the nonarid regions of North America. In addition to sites of heavy infestation, it is found in many brooks, streams, and small rivers, and can be seen near their banks. But it is not evident in the gardens, fields, and woods elsewhere in the countryside. Parlato, LaDuca, and Durham¹¹ found no caddis fly hairs on slides exposed more than six miles from the Niagara River, in spite of their great abundance at the river's edge. Exposure to caddis fly emanations of the general human population residing away from areas of its local concentrations must, therefore, be minimal. In my own experience, this minimal exposure is insufficient to cause symptoms in a patient unequivocally allergic to caddis fly. I believe that a relatively intense exposure is necessary to induce sensitivity to caddis fly and to excite allergic symptoms.

The May fly (*Ephemerida*), an aquatic insect except in the adult stage, is locally abundant in many areas, but is found only in the immediate vicinity of the water's edge. It develops in quiet bodies of water, such as ponds, lakes, and slow-flowing streams. Many people in lakeside cities and at fresh-water beaches and summer resorts are exposed to the dried and powdered pellicles of this insect.

In contrast to the sparsity of caddis flies and May flies in the general countryside are the ubiquitousness and relative abundance of butterflies and moths (*Lepidoptera*). Human exposure to the emanations of the *Lepidoptera* must, therefore, be much more common than to those of the *Trichoptera*.

From the preceding, it follows that human exposure to the *Lepidoptera* must be quite general. Exposure to the *Ephemerida* and the *Trichoptera* is

less widespread and is rather "spotty." Nevertheless, light exposure to the latter two orders cannot be entirely ruled out, except in arid and semiarid regions.

The coincidence of positive skin tests in the same patient to *Trichoptera* and *Lepidoptera*, reported by Parlato,⁷ and to *Trichoptera* and *Ephemera*, reported in the present article, may be interpreted, on the one hand, as the coexistence in the patient of separately specific sensitivities to the different insects or, on the other hand, as true relationships between the antigens of the three orders, with all the implications such relationships would present. Taxonomically, the *Trichoptera* and *Lepidoptera* are not too far removed from each other; hence, antigenic relationship may not be improbable. The *Trichoptera* and *Ephemera* are further apart biologically, so that antigenic relationship between them may be less likely. This problem certainly demands further careful investigation using modern experimental techniques—biologic, immunologic, and immunochemical—for studying the relationships between the antigens.

SUMMARY

A brief note is presented on the caddis fly as it occurs in the Niagara area. Directions are given for the collection and preservation of the insects and for the preparation of the extract. The typical caddis-fly-sensitive patient is described.

Skin tests with caddis fly extract were done on 623 patients suffering from symptoms of respiratory allergy. Of the total group, 34.5 per cent yielded definitely positive (moderate or marked) reactions and 65.5 per cent yielded indeterminate (slight) or negative reactions. However, 60 per cent (twenty-two out of thirty-seven) of the patients living in the immediate area of heaviest infestation (Fort Erie) showed moderate or marked reactions. The occurrence of these strong reactions decreased markedly as the distance of residence of the patients from the infested area increased and the exposure became less.

Fifty-seven patients skin positive to caddis fly have been treated with hypsensitizing injections of the extract. In ten of these, the caddis fly was the dominant factor in causing their symptoms; all ten lived in the immediate vicinity of the infested area. In the remaining forty-seven patients, other allergens (pollens, molds, May fly, etc.) were dominant, but caddis fly extract was also used in treatment because of known exposure.

The problems presented by the numerous patients who were definitely skin sensitive to caddis fly but who were not exposed to their emanations, so far as known, are discussed. The frequent occurrence of crossed skin reactions in a given patient to caddis fly, May fly, and to butterflies and moths raises the question of antigenic relationship between these separate orders of insects.

CONCLUSION

In the general countryside exposure of the human population to caddis fly emanations is insignificant. In the immediate area of heavy infestation by caddis flies, however, allergic sensitivity to this insect is quite frequent. Allergists should investigate the possible presence of these insects in the regions from

which they draw their patients and, if the insects are found in appreciable numbers, cases of caddis fly allergy should be anticipated and caddis fly extract should be included in their skin testing series.

From a practical point of view, and considering our present lack of knowledge regarding the antigenic relationships between *Trichoptera*, *Lepidoptera*, and *Ephemera*, I believe that specific hyposensitization with caddis fly should be undertaken in a patient skin positive to the insect only on the basis of known exposure.

Because of the fairly frequent occurrence of positive skin tests to caddis fly in patients having no known exposure to them, and because of the frequent crossed reactions in a given patient to the above three orders of insects, careful studies should be made with modern experimental techniques to determine whether these crossed reactions indicate the coexistence of immunologically separate sensitivities or antigenic relationships between the three orders.

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