

MAY FLY (EPHEMERIDA) HYPERSENSITIVITY

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TO ANYONE not familiar with the annual invasion of the myriads of May flies which occurs each summer in various parts of the United States, especially in the Great Lakes region, their abundance is unbelievable. In attempting to portray this, I can do no better than to quote a passage from a publication by Prof. James G. Needham of Cornell University, "Burrowing Mayflies of Our Larger Lakes and Streams"¹: "How abundant they are in all our large lakes and streams is well attested by the vast hordes of adults that appear in the air at the times of their annual swarming. They issue from the water mainly at night. They fly away to the banks and settle upon the shore vegetation. They cover the sides of buildings. They fly heedlessly into the faces of pedestrians. They settle upon the stream-side willows until their accumulated weight bends, and often breaks, the boughs. In the streets of riparian cities they fly to lights at night and fall beneath them in heaps upon the ground. Their bodies, crushed under the wheels of cars, render the rails slippery, sometimes impeding traffic. . . . Sometimes they stop the river steamers by clogging the machinery. No dweller by the shores needs to be convinced of their abundance." Figs. 1 and 2, taken at night near Port Clinton, Ohio, which is some forty miles east of Toledo on the south shore of Lake Erie, give some idea of the abundance of these insects.

The May fly belongs to the order *Ephemera*, named from the Greek word *ephēmeros*, meaning "lasting but a day." Various other names for them are "June flies," "lake flies," "shad flies," and "Canadian Soldiers." They are found along the shores of lakes and large rivers in various parts of the world. Isaak Walton mentioned them in his *Compleat Angler*, and I have seen them on the River Seine near Paris. In North America May flies are found most abundantly in the Great Lakes region, along the Mississippi, around the Finger Lakes in New York State, and among the Wisconsin lakes. The May fly larvae live on the mud bottoms of rivers and shallow lakes and, for this reason, are so very abundant along the shores of Lake Erie with its numerous shallow bays. About eighty-five known species of May flies occur in North America, divided into half a dozen genera. The most common of these are the brown drakes (*Hexagenia*) (Fig. 3). Other well-known species are the yellow drakes (*Pentagenia*) and the beautiful Mackerels (*Ephemerella*) (Fig. 4).

In 1929 I reported four cases of hypersensitivity to May fly emanations.² Since that time I have routinely tested all patients with seasonal

¹Read before the annual meeting of the American Society for the Study of Allergy, St. Louis, May 16, 1939.

hay fever and asthma for May fly sensitivity. In passing, it should be said that the time of the annual May fly invasion of the Great Lakes area is from the latter part of June until the first of August. The onset depends on how early the lake water reaches the proper sustained degree of warmth. It is apparent that the May fly season roughly parallels that of the grass pollens and English plantain, as well as the early mold spore season, thus adding to the complexity of diagnosis in early cases of seasonal hay fever and asthma in the Great Lakes area.



Fig. 1.—May flies on side of building at Port Clinton, Ohio.

In a series of 1,284 seasonal hay fever and asthma patients who were adequately tested, 95 (7.4 per cent) gave positive cutaneous reactions stronger than one-plus to May fly. Of these, 40 patients owed their symptoms all or in part to May fly sensitivity. Twenty of them reacted only to May fly and had no symptoms aside from those during the May fly season. The other 20 reacted only to May fly and ragweed pollen; they did not react to grass or plantain pollen or mold spores. These 40 patients were all treated with extracts of May fly or of May fly and ragweed pollen, and the results were quite satisfactory. In these 40 patients the cutaneous tests to May fly were usually three-plus or four-plus, and in every instance where passive transfer was attempted, the result was strongly positive.

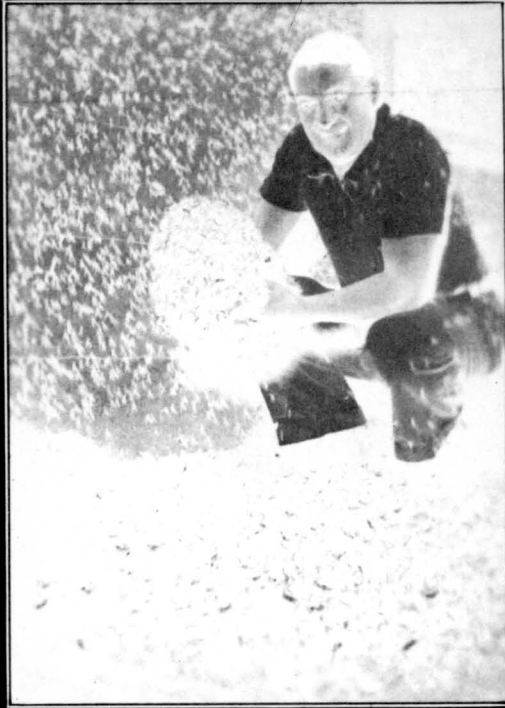


Fig. 2.—May flies expiring after nocturnal mating.

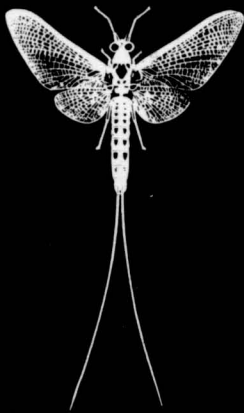


Fig. 3.

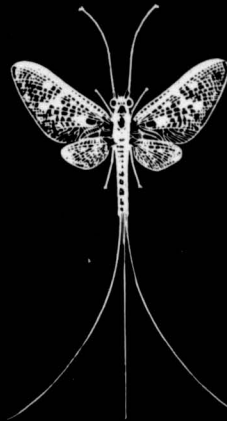


Fig. 4.

Fig. 3.—Adult male May fly, *Hexagenia bilineata*. (After Needham.)

Fig. 4.—Adult male May fly, *Ephemera varia*. (After Needham.)

The question will at once be raised about the other 55 patients showing positive reactions to May fly, and the specificity of their reactions. That they were specifically sensitive is attested by the fact that many of them were tested by passive transfer or by inhalation of powdered May fly; all so tested reacted positively. These 55 patients had all been exposed more than once to May fly contact and had developed specific hypersensitivity; however, they were not treated with May fly because they lived inland and could avoid exposure. In numerous instances, grass pollen sensitivity was more pronounced than May fly sensitivity, so that it was not considered necessary to treat with May fly. Because of the fact that glycerosaline insect extracts may at times give nonspecific cutaneous reactions, no cases were included that did not show at least a two-plus cutaneous test to May fly.

TABLE I
SUMMARY OF CASES

Total cases seasonal hay fever and asthma reviewed	1,284
No. cases giving two plus or stronger cutaneous reaction to May fly	95 (7.4%)
No. cases reacting to May fly only	20
No. cases reacting to May fly and other seasonal inhalant, usually ragweed	20
No. cases reacting to May fly but not requiring treatment	55
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	95

The following reports illustrate some of the cases encountered:

CASE 1.—V. E. L., male, aged 34 years, lives in Sandusky, Ohio, and in the summer works on a dredge in Sandusky Bay. He developed seasonal hay fever and asthma at the age of 15 years. Symptoms always begin coincident with the annual May fly invasion. During recent years, asthma has been very severe and lasts until October, and he has been hospitalized several times because of this. He was first seen by me in March, 1938, and gave a four-plus cutaneous reaction to May fly; there were no other reactors. Treatment with May fly extract gave complete freedom from symptoms last summer despite intense exposure to the insects during June and July. The patient is still being treated by the perennial method.

CASE 2.—J. S., male, aged 39 years, resides and works in Toledo, some 5 miles from Lake Erie. He was first seen on May 20, 1936, having severe asthma which had begun three days previously for the first time. The patient stated that he had had some hay fever in the fall of 1935. It was assumed that the patient's asthma was due to grass pollens, but tests with these were negative although he gave strong ragweed reactions. At a second visit, strong reactions were obtained to May fly, and it was then learned that the patient, an ardent yachtsman, had been scraping dead May flies from the hull of his boat just prior to the onset of his asthma. Passive transfer tests gave strong reactions to May fly and ragweed but negative reactions to grass pollens and mold spores. This man has been treated since the summer of 1936 with May fly and ragweed extracts. The result has been complete freedom from symptoms despite frequent exposure to May flies while sailing or working on his boat.

CASE 3.—R. DeM., male, aged 24 years, was first seen on June 15, 1935. The patient stated that since the age of 7 years he had had hay fever every year from August 15 until frost, with some asthma during sultry weather. When first seen he had been having hay fever for the previous two weeks, the first time he had ever had it in early summer. Cutaneous tests gave strong reactions to grass and ragweed pollens and to May fly. This man lives in Fremont, Ohio, some twenty miles south of Lake Erie, but had been accustomed in the summer to spend frequent week-ends at the beaches on the lake shore. Since 1935 he has been successfully treated for his seasonal hay fever and asthma with a mixture of grass and ragweed pollen extract. By remaining away from Lake Erie during the May fly season he has had no trouble from this source.

In the routine testing of the 1,284 cases of seasonal hay fever and asthma, cutaneous tests were always done with caddis fly extract as well as May fly extract. Ten patients gave positive reactions to caddis fly, about two-plus, but at the same time gave stronger cutaneous reactions to May fly. The late Dr. Salvatore Parlato, as is well known, wrote extensively regarding caddis fly (*Trichoptera*) hypersensitivity.³⁻⁶ Since our almost simultaneous publications in 1929, there was always a good-natured rivalry between us as to the relative incidence and importance of May fly and caddis fly hypersensitivity in the Lake Erie region. Shortly before his death, Parlato published a paper on May fly sensitization⁷ and in the summary stated that he did not believe the May fly to be as common an allergen as the caddis fly. From my observations over an equal period, I believe the reverse to be true. This divergence of opinion is explainable as follows: Caddis flies are undoubtedly more abundant at the eastern end of Lake Erie in the Buffalo area where Parlato made his observations. They inhabit the clean, sandy bottoms of lakes and streams. The May fly larvae, on the other hand, are burrowers, requiring mud and silt for their existence. This condition obtains ideally in the shallow bays at the western end of Lake Erie, where the water is only a few feet deep, rather than at the eastern end where the water is several fathoms deep. It is true that caddis flies are prevalent at the Toledo end of the lake, but they are so outnumbered by May flies as to be almost unnoticed.

In this study, routine testing was done by the cutaneous or the scratch method. The May fly is a good skin sensitizer, and scratch tests were depended upon to point out clinical hypersensitivity. However, in numerous instances, intracutaneous tests were done with both caddis fly and May fly, and in each case the reactions were usually equally positive by intracutaneous test, although the scratch test to caddis fly might be negative. This finding also was obtained by passive transfer in each instance attempted. Consequently, I believe there is an antigen common to both the May fly and caddis fly, as well as species-specific antigens, but I have not had an opportunity to prove this experimentally.

In order to understand how May flies produce allergic manifestations due to specific hypersensitization, a brief account of their life his-

tory is in order. There are two periods in the life cycle of the May fly: its underwater form, and its brief existence as the adult insect. In its underwater or larval form, the May fly exists as a tiny six-legged creature called a nymph, which breathes through gills and has strong jaws with which to burrow and chew (Fig. 5). During its aquatic existence which may last from one to three years, the nymph undergoes successive moults. After several moults, there appear on the body four little sacs which are the beginning of the wings. With each moult these wing sacs grow larger, until finally on some warm summer evening at the end of the underwater life, the nymph floats to the surface, splits open along the back, and after scarcely a second's pause, the winged May fly emerges (Fig. 6).



Fig. 5.—Dorsal view of nymph, *Hexagenia bilineata*. (After Needham.)

Most of the May fly species go through another moulting after acquiring wings. After flying a short distance to the land or some convenient object, the May fly alights and sheds its skin again, this time a thin layer coming off from all parts of the body, including the wings. This shed skin, known as the pellicle (Fig. 7), is very friable and delicate. When the May flies are swarming, myriads of these pellicles may be seen adhering to walls, screens, posts, or trees, where they have been deposited.

It is this friable pellicle that is chiefly responsible for the production of allergic sensitization. It is easily fragmented by a breeze, so that its particles are carried long distances to be inhaled. Unlike the caddis fly and other insects, the May fly sheds no hairs or scales from its wings, so that it must be particles of epithelial masses from the pellicles which constitute the May fly allergen. This has been proved repeatedly by means of conjunctival and inhalation tests.

The fully developed, winged May fly has but one duty to perform during its brief life—to reproduce its kind. This is done during the flying dance, the most conspicuous event in the life of the adult insect.

In the early twilight the fly comes forth, full-fledged, joins its millions of companions in the swarming mass of insects where the males fertilize the females, which drop their masses of eggs on the water's surface (Fig. 8). The eggs settle slowly to the mud bottom of the stream

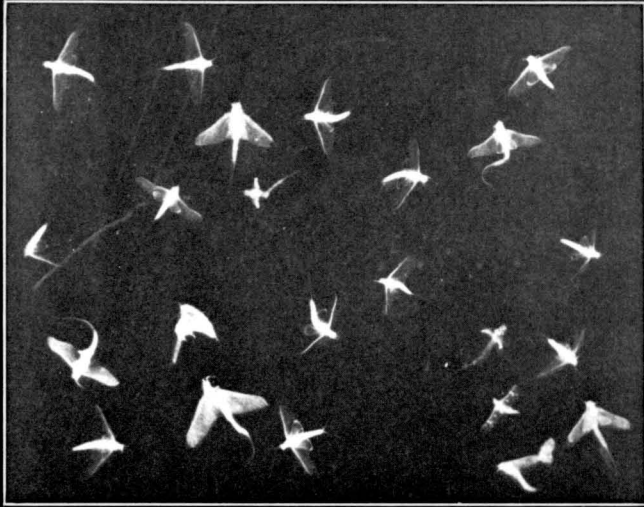


Fig. 6.—Adult May flies in flight.

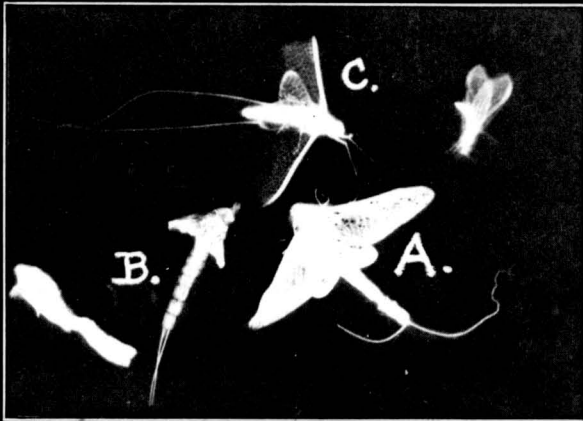


Fig. 7.—A, Adult May fly before moulting; B, shed skin or pellicle; C, fully matured adult insect.

or lake, and a nymph eventually hatches from each to perpetuate the species. Its purpose in life accomplished, the adult May fly dies in a few hours, as it lacks suitable mouth parts with which to take food. Thus it fittingly lives up to its name, meaning "ephemeral," lasting but a day.

Extracts for testing and treatment are made as follows: In the morning adult May flies in any desired quantity are readily scooped up where they have fallen under a light or near the water's edge after their nocturnal mating. They are dried under gauze in the sun for a few days. They are then pulverized in a mortar, washed with some fat solvent, and extracted with buffered saline for 24 hours. My usual stock solution is 3 per cent, or 1:30, and from this are made various dilutions as weak as 1:100,000. The degree of May fly sensitivity and pollen sensitivity is comparable, so that the same precautions are taken when testing or treating with May fly extract. In my experience, treatment of May fly-sensitive patients has been highly satisfactory from the standpoint of relief and prevention of symptoms, possibly because of the specificity of the allergen. Then, too, I have treated a number of patients by the perennial method and have gained the impression that permanent clinical immunity can be brought about in a much shorter time than is the case with perennial pollen treatment.

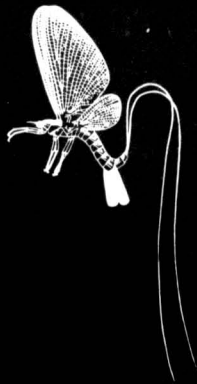


Fig. 8.—Adult female, hovering with egg packets extruding. (After Needham.)

In conclusion, May fly hypersensitivity is quite common among allergically susceptible individuals who are exposed to these insects by reason of residence near the Great Lakes or other large fresh-water bodies such as the Mississippi and the lakes of New York and Wisconsin. Such persons, evidencing symptoms of seasonal hay fever and asthma, should always be tested routinely for May fly sensitization, as this may exist alone or accompany pollen and other seasonal sensitivities.

SUMMARY

The abundance and distribution of May flies are described.

In a series of 1,284 patients with seasonal hay fever and pollinosis who were adequately tested, 95 (7.4 per cent) reacted to May fly. Of these, 20 reacted to May fly alone, and 20 to May fly and some other inhalant, usually ragweed pollen. Three illustrative cases are cited.

A comparison of May fly and caddis fly sensitization at the western end of Lake Erie is given and the opinion advanced that there is an antigen common to both the May fly and the caddis fly, as well as species-specific antigens for both.

A brief account of the life cycle of the May fly and its mode of production of specific sensitization is given.

The method of making May fly extract for testing and treatment is described.

REFERENCES

1. Needham, James G.: Burrowing Mayflies of Our Larger Lakes and Streams, Bull. Bur. Fisheries, 1917-1918, **36**, Document No. 883, issued July 17, 1920.
2. Figley, Karl D.: Asthma Due to the Mayfly, *Am. J. M. Sc.* **178**: 338, 1929.
3. Parlato, S. J.: A Case of Coryza and Asthma Due to Sand Flies (Caddis Flies), *J. ALLERGY* **1**: 35, 1929.
4. Parlato, S. J.: Sand Fly (Caddis Fly) as Exciting Cause of Allergic Coryza and Asthma: Its Relative Frequency, *J. ALLERGY* **1**: 307, 1930.
5. Parlato, S. J.: Studies of Hypersensitiveness to the Emanations of Caddis Flies (Trichoptera), *J. A. M. A.* **102**: 910, 1934.
6. Parlato, S. J.: Studies of Hypersensitiveness to the Emanations of the Caddis Fly (Trichoptera), *Ann. Int. Med.* **7**: 1420, 1934.
7. Parlato, S. J.: The May Fly as an Exciting Cause of Seasonal Allergic Coryza and Asthma, *J. ALLERGY* **10**: 56, 1938.

DISCUSSION

DR. W. W. DUKE, Kansas City, Mo.—The two discoveries, one by Dr. Figley, the other by our friend, the late Dr. Parlato, represent a very interesting advance in the study of allergy. We found in our earlier studies that people could become sensitive to insect bites or stings and react excessively to them. I remember vividly one of my first patients of this sort, a case brought to me in complete shock, with a history of angioneurotic edema, vomiting, and diarrhea to such an extent that he was almost dehydrated. His relief after adrenalin and the oral administration of water containing salt and sugar seemed almost magic.

The type of sensitivity which Dr. Figley describes is of an entirely different nature from the above and reminds one more of sensitiveness to ectodermal substances or other inhalants.

There is an interesting difference between Dr. Figley's fly and Dr. Parlato's fly in that, as the author mentioned, scales of the insect cause the reaction in Parlato's patients, while in Figley's, the excitant is found in fragments of the dried pellicles.

In Kansas City we very seldom have this type of insect allergy. One summer, however, we had almost a plague of scale-bearing flies. I found several cases in this one year. I have had several patients who lived in the Mississippi bottom lands further north than Kansas City.

I have wondered why we do not commonly find grasshopper cases so constantly and in such quantity as Figley finds May flies, but I should think there would be areas where this type of sensitivity to grasshoppers would exist.

I have observed one case of sensitiveness to the common housefly. In this case, the bite of a housefly would cause a delayed inflammatory reaction at the site of the bite. This was followed by a debilitating systemic illness associated with loss of weight if the fly bites were numerous.

This study has added an important chapter to our knowledge of allergy, and in areas where insects prevail at certain seasons, it should solve the source of many cases of nasal and bronchial allergy which would otherwise remain a mystery.

DR. SAMUEL M. FEINBERG, Chicago.—Even in Chicago we have had some experience with May flies. One or two of our patients have come from outside Chicago.

I should like first to ask Dr. Figley one question: How far inland may we expect to have trouble?

Then I should like to call attention to the fact that in part answer to Dr. Duke's question, I think we cannot expect grasshoppers and similar insects to cause allergic reactions because most of these insects do not have anything in the way of scales or hairs or moulting of a type that Dr. Figley has described; in other words, there is nothing much that can get in the air to be inhaled into our respiratory tracts.

These emanations are apparently applied to the *Ephemera*, the *Lepidoptera* (butterflies and moths), and the *Trichoptera*, of which the caddis fly is an example. We are likely to be led astray unless we look at the thing from the biologic standpoint.

Also I should like to ask Dr. Figley this hypothetical question concerning the relationship of these flies or insects antigenically. He talked about the caddis fly. What about the butterfly and moth, and what about silk? We obtained a slight impression clinically that some of these fly cases inter-react with silk.

To cite an example briefly: a young man who has seasonal symptoms, eye symptoms, apparently allergic, from year to year in the summer, gave a very marked reaction to silk on scratch test. I could not correlate this thing at all until I began to test with butterfly, moth, May fly, and caddis fly extract, and I also got a reaction to these insects.

I should like to ask one question for information. In Chicago we have used May flies that we caught under lamps and extracted them. Of course, they are through moulting at that time, and I wonder whether Dr. Figley tries to get them before they shed their pellicle in order to get a better extract or whether he gets it from the adult fly.

DR. ROBERT L. BENSON, Portland, Ore.—Dr. Figley and Dr. Parlato have both demonstrated very nicely that the inhalant effects of insects are examples of true allergy of the type which Coea and Walzer and their associates have designated atopy, and, of course, they get universally good passive transfers.

This is quite different with the bites and stings of insects, which produce a different type of reaction. The essential reaction with these bites and stings occurs within 24 to 48 hours, and, as one would expect, the passive transfer is either absent or very difficult to get with these biting and stinging insects.

I have, on certain occasions, obtained a passive transfer with the biting and stinging insects, but more often it has failed. This demonstration of both Dr. Figley and Dr. Parlato, I think, is valuable not only for its practical benefit but also for bringing out this principle.

DR. HOWARD OSGOOD, Buffalo.—Dr. Parlato really should be here to speak on this; his untimely death was certainly tragic. I test always with May fly and caddis fly and also with silk. Like Dr. Figley, we

often find reactions to both caddis fly and May fly, but not invariably, so that the antigen cannot be identical. I would also corroborate Dr. Feinberg's remarks that we find not infrequently reactions to silk in such individuals. My impression is that, being in the midst of an insect district, as you might say, we are dealing with individuals who are sensitive to a group of insects, very much as we find sensitivity to a group of cereals, for instance, in skin testing with foods.

I think it might be interesting if Dr. Figley made up his dilutions on a protein nitrogen basis, because the protein constituent of extracts of these different insects varies quite widely.

DR. MILTON B. COHEN, Cleveland.—When two equally good men, Dr. Figley at one end of Lake Erie and Dr. Parlato at the other, disagree on the relative importance of two flies, it behooves one of us who lives just halfway between to comment on the relative importance of the May fly and the caddis fly.

I see not nearly as many May flies around Cleveland as Dr. Figley sees up in his territory. Most of the clinical cases of May fly sensitivity I see come from the lower end of the lake, and the only ones I have ever seen that were May fly, and May fly alone, came from the Lakeside or such area around the end of the lake, with the shallow water that Dr. Figley has described.

In Cleveland I have never seen a case that I could say myself was a pure case of caddis fly sensitivity. I do not know—they certainly must exist; but, since I do get reactions to caddis fly and May fly simultaneously, and since the patients that I have whom I suspect of having difficulty are exposed to many more May flies than caddis flies, I have simply concluded without any experimental evidence that these May fly cases are just May fly cases. I have treated them with May fly extract, and good results follow treatment.

DR. LEON UNGER, Chicago.—The other day I met a physician from Keokuk, Iowa, who told me about a whole series of very interesting cases. This man has done some work on allergy and has skin-tested a lot of patients who come from a power plant near Keokuk. He said that all up and down the Mississippi River where they have these power plants they have swarms of flies which they call "river flies." I do not know what "river flies" are, and I am asking for information.

He said they sweep up bushels of these flies at the power plants, and that almost every worker sooner or later becomes sensitized to these flies and develops rhinitis or bronchial asthma, very severe bronchial asthma in a good many cases.

This physician has made extracts of these "river flies" and injected them into the patients, and he claims to get splendid results.

DR. CLARENCE K. WEIL, Montgomery.—Since the "river fly" has been mentioned, I want to speak briefly of another insect which actually may be the same one. On the hydroelectric dams in Alabama is found a genus of midges, belonging to the family *Chironomidae* and known as the tanytarsus. They are so abundant that they can be gathered easily by wiping off the lights or sweeping the floor. We have had one patient who gave a positive reaction both by testing and passive transfer tests and excellent results following treatment. One winter the patient returned to the dam and remained free of symptoms until he cleaned a

dynamo to which were attached large numbers of the dead insects. As this case will be discussed in more detail in my paper, I shall limit the discussion simply to mentioning the possible importance of this insect. The citrus white fly may also be of importance in causing allergic symptoms.

DR. FIGLEY.—With reference to Dr. Feinberg's question as to how far inland these flies may cause trouble—as the map will show, Toledo is situated at the lower end of the Maumee River, or the beginning of the Maumee Bay, which is about five miles inland from the lake proper. Those persons, whom Dr. Cohen mentioned, who live on the shores of Maumee Bay and farther east along the lake shore toward Cleveland are definitely exposed.

Most of the patients that I see come from Port Clinton and Sandusky. Strange to say, we do not have many cases in metropolitan Toledo itself because it is some five miles from the lake. Many patients who do come from Toledo, as a rule, live on the shores of Maumee Bay.

I have had one or two patients who have lived in town and, without ever seeing these insects, have had definite seasonal hay fever symptoms. On the other hand, when a strong northeast wind carries these insects inland, people living 20 and 30 miles back from the lake are affected. Also I saw May flies once as far south as Lima, Ohio, 70 miles away.

Dr. Feinberg, as to the relationship antigenically between moths, butterflies, etc.—these cases I have reported have all been tested with moth or butterfly extract, and I have failed so far to get a reaction.

Dr. Feinberg also inquired whether the extracts were made from the pellicle or the adult fly. It is much easier and better to make the extracts from the adult fly because the pellicles are rather difficult to collect. You have to pick them one by one from posts; furthermore, the pellicle contains only about one-tenth the nitrogen that an adult fly does. There is plenty of antigen in the pellicle to cause trouble, but I did not bring out that these May flies live only from 36 to 72 hours. After the adults die, they dry very rapidly, and their dried fragmented bodies add to the total amount of epithelial scales in the air.

Doctor Unger inquired whether the so-called "river flies" so prevalent at Keokuk were the same as May flies. They are one and the same. The Bureau of Fisheries has long been interested in May flies because their larvae constitute a major part of the diet of the fish in the Great Lakes and the larger rivers. Professor Needham's outstanding study, "Burrowing Mayflies of Our Larger Lakes and Streams," made for the Bureau of Fisheries years ago was based on material obtained mainly from the Mississippi dam at Keokuk.