

SEASONAL HAY-FEVER

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The amount of work which has been done on the subject of hay-fever, and the voluminous literature which has accumulated so rapidly in the last few years, have done much to place the care of this disease on a satisfactory basis and to permit hay-fever to be classed, at last, as a curable disease. Those who have had most to do with this work are the first to admit that there is much yet to be learned and that the methods employed are not yet entirely perfected. Since no reports on this work have appeared from this locality, and because our findings do not in every particular parallel those reported by some observers, we are venturing to present the observations of the last two years, covering a series of ninety patients.

These patients have all been resident in northern Texas and, with one exception, within a radius of 100 miles of Dallas. Eighteen, or 20 per cent., of them developed the disease in other states, but all have had one or more attacks in this vicinity, and all have been under observation during their hay-fever season.

The percentage of the local population affected is not definitely known, but from our observation we believe that the number is certainly not less than 1 per cent.—the figure obtained by the American Hay-Fever Prevention Association. The summer temperature ranges high, warm weather persisting well into September. Summer humidity is variable, but rarely high. The winters are mild, freezing temperatures being infrequent. "Killing frosts" rarely occur until November. The growth and pollination of plants, therefore, extend over the greater part of the year, and, save from late October until early February, some pollen may always be found.¹ In spite of this fact, there have been found in this series only six vernal cases, and three combined vernal and autumnal; the other eighty-one (90 per cent.) have been of the typical autumnal type. This is far in excess of the percentage reported by Scheppegegrell.² In 1,000 cases, he found 38 per cent. of the autumnal type and 42 per cent. of the combined vernal and autumnal. We are at a loss to account for this difference. That our figures actually represent, approximately, the relative frequency of vernal and autumnal cases in this locality, we do believe, for observation over a period of two years has shown surprisingly few cases during the spring months, a striking contrast to the large number seen in the fall.

The sexes have been fairly equally represented, there being 44 per cent. male and 56 per cent. female.

The age at onset has varied from infancy to 45 years. Grouped by decades, the percentage found in each decade is: from 1 to 10 years, 10; 10 to 20, 20; 20 to 30, 45; 30 to 40, 20, and 40 to 50, 5.

The duration of the disease has varied from one to twenty-eight years. No tendency to spontaneous recovery can be seen in the fact that 40 per cent. of this series had had the disease fifteen or more years.

Thirty patients (33⅓ per cent.) stated that father or mother, sister or brother had either hay-fever or

asthma. In seventeen instances, the familial disease was hay-fever; in the remaining thirteen, asthma.

ETIOLOGY AND SYMPTOMS

As predisposing causes, three patients date the onset of their hay-fever to a summer in which they did much swimming, the first diagnosis being, in each instance, a nasal infection. Two relate their first attack directly to the ingestion of honey. In no others could any causal relationship be established. One patient states that he has a marked exacerbation of symptoms on eating watermelon during the hay-fever season. It can be eaten at other times without ill effect. One vernal case presents a similar condition, save that the offending material is, in this instance, wheat. This patient gave, in addition to the positive pollen reaction, a slight reaction to wheat proteose. Pollen injections given as a preseasonal prophylactic did not secure relief from symptoms until wheat was removed from the diet. The symptoms then immediately subsided. This patient takes wheat without restriction and without ill effect at all other times. This phenomenon has been mentioned by Walker.³

Thirty two per cent. of this series of patients stated that at some time during the season they had asthmatic breathing. Of these, 18 per cent. had only nocturnal dyspnea, while 14 per cent. claimed that difficult breathing occurred both day and night during at least part of the season. In two instances, the dyspnea was so severe as to justify the diagnosis of asthma. The pollen relationship had been entirely overlooked.

Of the nine patients showing vernal symptoms, five gave reactions to corn pollen, one to elm (*Ulmus americana*), one to white ash (*Fraxinus americana*) and two to cottonwood (*Populus angustifolia*). All those reacting to corn pollen gave histories of intimate exposure and of relief from symptoms by removal a very short distance from the flowering corn. A child who gave a typical cutaneous reaction to ash pollen secured relief in the subsequent season after the cutting down of a large ash tree in the yard. The symptoms in the four cases due to tree pollens fell within the period limited by the latter part of February and the early part of April. Three of the patients who were sensitive to corn reacted also to ragweed, and presented pictures of combined vernal and autumnal hay fever. Although this series is entirely too small to justify any conclusion, the entire absence of any grass pollen cases, save those due to corn, is interesting. The figures are also in decided contrast to the figures reported from other localities. We have seen no cases due to winter cedar, such as have been reported about Austin.

The autumnal cases, with striking uniformity, begin about August 20, and continue until early October. Three patients asserted that they had no symptoms until September 1. They gave only slight cutaneous reactions and were possibly only slightly sensitive, and reacted to atmospheric pollen only in relatively large amounts. Because of climatic conditions which caused late pollination in 1921, all patients were free of symptoms until September 1, following which they pursued their usual course. Three patients stated that their symptoms developed before August 15. These gave a history of exposure to dust or other respiratory irritant, which apparently produced a rhinitis, which, in turn, ushered in the hay fever. The symptoms from the two

1. The flora of this locality is described by Scheppegegrell: Hay Fever and Asthma, Philadelphia, Lea & Febiger, 1922.

2. Scheppegegrell (Footnote 1), p. 126.

3. Walker, I. C.: Frequent Causes and Treatment of Seasonal Hay-Fever, Arch. Int. Med. 28:71 (July) 1921.

conditions were not differentiated. Eight patients stated that they had, following their hay-fever season, a continued sneezing, with rhinorrhea, which persisted a variable length of time. In one instance, the first attack experienced had been preceded by much swimming and diving and, instead of clearing up early in October, it persisted until the following spring, with practically no interruption. The diagnosis of hay-fever was not made until subsequent seasons, when typical seasonal onset and duration made the diagnosis apparent. It is evident that these patients had an infection of the upper respiratory tract complicating their hay-fever. Fifteen patients stated that they developed sneezing, lacrimation and rhinorrhea at any time of the year on exposure to dust or other respiratory irritant. This exaggerated sensitiveness of the nasal mucosa appears to be a result of repeated attacks of hay-fever, and requires, often, careful differentiation from true, perennial hay-fever.

It has been an interesting observation that of all the ninety patients in this series, only twelve had escaped intranasal operative measures of one kind or another; and one patient had been operated on six different times. Many of these operations were undoubtedly indicated for the relief of obstruction or to promote drainage, but none was followed by any improvement in the hay-fever.

Two patients gave histories of bronchial asthma at other than the hay-fever season. In one of these, all attacks of asthma had ceased on the development of the pollen sensitization, and during the last five years—the duration of the pollen sensitization—there have been no asthmatic attacks at any time, and no cutaneous reaction other than that to the pollen can be elicited. In the other patient, the asthma and hay-fever were apparently independent, the one being due to casein, the other to ragweed pollen.

One patient had also a chronic eczema, and one an urticaria; and one stated that wheat flour precipitated an attack when it reached her nasal mucosa, as it did when she was engaged in making bread. All three of these gave negative cutaneous reactions, except to ragweed pollen.

It is probably worth mentioning that in two patients, not included in this series, who suffered from typical bronchial asthma, their attacks were ushered in by a brief period of sneezing, lacrimation and rhinorrhea, which disappeared at the onset of the dyspnea. They did not react to any pollens.

The eighty-one autumnal cases were all positive to ragweed pollen. Their onset and duration corresponded to the flowering of ragweed in this locality, and treatment with ragweed pollen has given the only satisfactory results obtained. Giant ragweed grows luxuriantly here. It reaches a height of from 8 to 10 feet, produces a great amount of pollen, and, because of general indifference to the growth of weeds, is found generally distributed.

Of these eighty-one autumnal cases, fifty-four, or 60 per cent., of the total series showed multiple sensitization. Forty-four of the patients were sensitive to one or more *Compositae*, the most frequent reactions being to goldenrod, yellow daisy and sunflower. Eight were sensitive to pollens of other botanical groups, in addition to several *Compositae*; while two gave reactions to ragweed alone of the *Compositae*, plus members of another botanical group. These were the combined vernal and autumnal cases. These figures are in

general accord with those of other observers who have found multiple sensitization the rule rather than the exception.

TREATMENT

Because of the striking relation of the onset and duration of symptoms to the pollinating period of ragweed, and because of the wide dissemination of ragweed pollen by air currents, while goldenrod, daisy, sunflower and other similar pollens are not wind borne, treatment has been conducted in all patients under our control with ragweed pollen alone. In two instances in which the cutaneous reactions to sunflower were marked, treatment with this pollen was instituted by the attending physician, with no improvement.

Our first work was done using the scratch method, according to the technic adopted by Walker,⁴ in which a number of small cuts were made on the flexor surface of the forearm, avoiding the drawing of blood. On each cut, we placed a pollen solution, and the reactions were read at the end of thirty minutes. In the majority of instances, this method was satisfactory; but it was soon found that occasionally an individual who gave a typical history of autumnal hay-fever gave no reactions to any pollens used by the cutaneous method. These patients were then given approximately 0.01 c.c. of pollen solution, intradermally. In our series, there were nine giving typical reactions following the intradermal injection who gave absolutely negative reactions to the pollen applied to scratches. Five others gave typical reactions to the intradermal pollen and only slight reactions to the scratch method. In several instances, 1:100 pollen solution gave a typical reaction when used intradermally; while a 1:50 pollen solution was followed by a negative reaction by the scratch test. In three instances, there were well marked reactions to other *Compositae*, with none to ragweed, when the scratch method was used; while, with intradermal injection, the reaction to ragweed was pronounced. Treatment of these patients with ragweed pollen has given fully as satisfactory results as with those whose cutaneous reactions to ragweed were quite typical.

The question naturally arises as to whether these patients have a less marked sensitization, which accounts for their more feeble skin reaction. Our series is too small for definite conclusions, but we have been unable to note any better response to treatment in these than in others, who gave well pronounced reactions to the scratch method. We are inclined to believe that the difference is one of skin sensitiveness rather than a constitutional variance. In any event, we have been forced to conclude that we cannot rely entirely on a negative scratch test. In one instance, a patient gave a history of hay-fever which occurred irrespective of season. Questioning elicited the fact that the condition was worse during August and September. Scratch tests were negative. Intradermal injection of ragweed pollen, however, gave a typical reaction. Treatment with ragweed pollen plus an autogenous vaccine gave a most gratifying result. Dependence on the scratch tests alone would, in this instance, have led us far astray.

We have observed one asthmatic who was desensitized by her attacks, and the reaction, which was typical before the attack, was entirely absent for a brief and variable period after the attack.⁵ This

4. Walker, I. C., and Adkinson, J.: J. M. Res. 37: 287 (Nov.) 1917.
5. Schloss, O. M.: Allergy in Infants and Children, Am. J. Dis. Child. 19: 433 (June) 1920.

phenomenon has not been seen in any hay-fever patients.

A condition which is fairly frequent in this locality and which must be differentiated from true hay-fever is the so-called vasomotor rhinitis. These cases may present the symptoms and the intranasal appearance of true hay-fever. They are, however, perennial in type, or, at least, quite irregular in their time of onset and duration; they are not improved by rainy weather, and they are usually more severe and more frequent in the winter months. Twenty-six patients fall into this class. Eight of these showed a sensitization to some food protein, and were relieved by its elimination from the diet. The remaining eighteen gave no typical reactions to any cutaneous tests. Because many of them gave slight reactions to bacterial proteins and a few of them related their condition to a "cold" which immediately preceded it, autogenous vaccines were used. The results have not been brilliant. Nine, or 50 per cent., of them showed no improvement; five were completely relieved; while the remaining four received moderate degrees of relief.

We desired to start treatment from two to two and one-half months before the onset of the season, so that treatment might be completed before the season began. An interval of at least five days between injections was considered advisable. During the season just past, treatment of the first patient was begun, June 1, and of the last, July 26. Those who were taken late were treated under protest, and little improvement was expected.

The time of the first injection determined the interval between doses. In those beginning late, the treatment was given every forty-eight hours. The longest interval in any case was five days. Much to our surprise, those who began treatment late (sixteen began after July 10) obtained almost as satisfactory results as those starting earlier. From our limited observation, we are not convinced that the long interval between doses is necessary. Results are shown in Table 1.

TABLE 1.—RESULTS OBTAINED WITH DIFFERENT INTERVALS BETWEEN DOSES

IMPROVEMENT				
	75%	50%	25%	None
5 days.....	3	16	5	5
4 days.....	6	16	5	5
3 days.....	0	4	3	0
2 days.....	3	4	9	0

CONSIDERATION OF RESULTS

We have become thoroughly convinced that the best results are obtained when the largest dosage is reached just at the onset of the season. Those whose treatment we directed were carried through to the actual beginning of the season, but, among those treated by others, eight were hurried through, and treatment was completed at periods varying from one month to two weeks before seasonal onset. These, without exception, showed little or no improvement. We are convinced that the desensitization secured is extremely fugitive, and that cessation of treatment sometime before pollination begins permits the patient again to become sensitive and to react as usual to pollen.

With this in mind, we have, with three patients whose treatment had been carried up to August 20, continued treatment through the season, using one-half the largest preseasonal dose. Two of these patients had been treated the previous year without seasonal

treatment and had secured only fair results. With seasonal treatment, this year, they were approximately 90 per cent. improved. The third patient obtained equally satisfactory results.

We have not been able this year to determine any difference in results in the eighteen who had been treated the previous season, except in the two just mentioned, who, this year, received treatment throughout the season. Of the other sixteen, twelve were improved approximately 50 per cent. each year, while the other four claimed 75 per cent. improvement.

A year ago, we felt that the dosage recommended and supplied by those engaged in the preparation of pollen for use in treatment was not carried to a sufficiently high point. In that year, two patients were

TABLE 2.—RESULTS OBTAINED BY THE USE OF 1:100 POLLEN COMPARED WITH RESULTS WHEN LESS WAS USED

	75%	50%	25%	0%
1: 100 pollen.....	9	28	12	2
1: 500 pollen.....	3	12	10	3

given, for their last three injections, 1:100 pollen solution in 0.1, 0.2 and 0.3 c.c. doses, respectively. We felt that the results obtained were better than in the others who received less pollen; we have used 1:100 pollen this year in fifty-one cases. The largest dose used has been 0.3 c.c. Nine of the patients showed an improvement of 75 per cent. or more; twenty-eight were more than 50 per cent. improved; twelve claimed no more than 25 per cent. improvement, and two secured no relief at all. Of those whose largest dose was 0.4 c.c. of a 1:500 solution, only three received 75 per cent. or more improvement; twelve between 50 and 75 per cent.; ten between 25 and 50 per cent., and three were not improved at all. Results are presented in Table 2.

Of the entire series, only one patient gave any reaction to the pollen injections. She developed local edema and hyperemia, together with a sharp attack of hay-fever and dyspnea after a dose of 0.3 c.c. of 1:1,000 ragweed pollen. The dosage was carried only slightly further, and her improvement was approximately 50 per cent. Through a misunderstanding of instructions, one physician administered at the first injection 0.9 c.c. of 1:10,000 ragweed pollen. Three days later, he gave the same amount of 1:5,000, then 1:1,000; and, on the ninth day after the first dose, she was given 0.8 c.c. of 1:500 dilution. Strange to say, she showed neither local nor general reaction at any time.

Of the seventy-nine patients treated with ragweed pollen, fifty-two, or 65.8 per cent., received more than 50 per cent. improvement. Not one was completely cured, if we understand cure to mean an absolute absence of any symptom. While the failure to secure complete cures is disappointing, the value of pollen treatment as an ameliorating agent is proved. When it is remembered that treatment was begun on sixteen patients after July 10 (two as late as July 26); that eight completed their treatment from two to four weeks before the season began, and that twenty-eight received less pollen than we feel should be given, the results justify the work. We believe these results could be much improved if the patients were under constant supervision of one giving attention to this work.

Treatment was not begun during the season in any instance. We have felt that the relief to be expected

was slight and that failures from this method would militate against the use of the preseasonal treatment. We have preferred thus to limit our work until more definite information is available.

SUMMARY

1. Autumnal hay-fever is quite common in northern Texas; while vernal cases are rare.

2. In autumnal cases studied, the patients, without exception, have reacted to ragweed.

3. No case due to grass pollens (except corn) has been seen.

4. Onset and duration of autumnal attacks corresponds to pollination time of ragweed, extending from about August 20 to October 10.

5. Sixty per cent. of all cases seen showed multiple sensitization; 49 per cent., were sensitive only to members of the same botanical group.

6. No patients were treated with combined pollens. When multiple sensitization was found in autumnal cases, ragweed pollen was used.

7. The intradermal method of testing proved more dependable than the scratch method.

8. Best results were obtained from treatment when doses were given at a four-day interval.

9. Treatment should not be discontinued before the beginning of the season. Better results probably follow when treatment is continued through the season.

10. Patients given 1:100 pollen obtained somewhat better results than those stopping with smaller dosage.

11. Reactions, local or general, are infrequent if the dosage is carefully graduated.

12. Seasonal treatment alone was not used.

13. In 65.8 per cent. of all autumnal cases, there was more than 50 per cent. improvement; and in 15.2 per cent. more than 75 per cent. relief from symptoms was claimed. No complete cure was obtained.

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A STUDY OF ONE HUNDRED CASES
DIAGNOSED AS HYPERTHYROIDISM

WITH PARTICULAR REFERENCE TO DIFFERENTIATION,
SYMPTOMATOLOGY, THE VEGETATIVE NERVOUS
SYSTEM, BASAL METABOLISM, AND THE
SUGAR TOLERANCE AND KOTTMANN
TESTS *

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A special opportunity was afforded at U. S. Veterans' Hospital No. 76 for this study on account of the large amount of material found in the neuropsychiatric and tuberculosis sections, and the excellent laboratory facilities offered. Our patients were, for the most part, from the Great Lakes districts, and it was significant that all of them presented a palpable and noticeable enlargement of the thyroid gland. This enlargement, with some symptoms and signs of hyperthyroidism, suggested the diagnosis of hyperthyroidism until further investigation disclosed otherwise. The ages of the patients ranged between 22 and 32 years, with an average of 25 years.

All patients referred to our department underwent an additional physical examination in which special note

was made of eye signs, vegetative nervous system manifestations, thyroid enlargement and pulsations, heart rate at rest and after exercise, and blood pressures. Mental and neurologic studies were made. A careful inquiry into the subjective symptoms with previous history was always an essential part of the investigation. Basal metabolic determinations by means of the Sanborn-Benedict apparatus, two ten minute tests being made; blood sugar estimations before and after the ingestion of 100 gm. of glucose, according to the method of Folin and Wu;¹ and the Kottmann reac-

TABLE 1.—FINAL DIAGNOSES

	Number
1. Hyperthyroidism	30
2. Hypothyroidism	6
3. Neurasthenia	33
4. Neurocirculatory asthenia	4
5. Hysteria	3
6. Chronic war neurosis	10
7. Interstitial pneumonia following gassing	5
8. Chronic active pulmonary tuberculosis	1
9. Valvular heart disease, aortic regurgitation	1
10. Cardiac arrhythmia, extrasystoles	1
11. Chronic myocarditis	1
12. Dementia praecox	3
13. Manic-depressive psychosis	1
14. Mental deficiency	1

tion² as outlined personally by Drs. Petersen and Levinson, were carried out as routine procedures in each case. A series of Goetsch and thyroid feeding tests also was made.

It was possible to keep under observation for a prolonged period of time a majority of the patients, thus giving an opportunity to study them further, to obtain accurate pulse and temperature records, and to repeat whatever tests were deemed necessary.

The final diagnoses grouped themselves as in Table 1.

From this table it is seen that the number of hyperthyroid cases, determined as such, approximated only about a third of the total number, whereas the psychoneurosis and neurosis group made up 50 per cent. Two of the interstitial pneumonia cases, three of the hypothyroid and five of the hyperthyroid were definitely complicated by a psychoneurosis of the neurasthenia type.

The subjective symptoms are given in Table 2.

The complaints of the hyperthyroid patients impressed one more definitely, and were usually clear cut, while those of the psychoneurotic patients abounded in vagueness, were quite numerous, and were frequently irrelevant to any ascribable pathologic condition. The psychoneurotic patient was usually introspective and circumstantial in his detail of affairs. Apprehension was frequently a noteworthy feature of the former group, which showed itself to one at first glance possibly on account of the stare of the eyes so common to these patients.

The nervousness which was by far the most common complaint was often ill defined and inexplicable by the patient. By twenty-two patients it was explained as being easily excited; by six, as trembling of the hands, and by eight as a fear reaction. These definite subdivisions were more frequent in the hyperthyroid group.

Fatigability was pronounced in both groups, but here again it appeared much more real in the toxic thyroid subject, in whom it was also more apparent.

1. Folin, O., and Wu, H.: *J. Biol. Chem.* **41**: 367 (March) 1920.
2. Petersen, W. F.; H'Doubler, F. T.; Levinson, S. A., and Laibe, J. E.: The Kottmann Reaction for Thyroid Activity, *J. A. M. A.* **78**: 1022 (April 8) 1922.

* From U. S. Veterans' Hospital No. 76.