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ORIGINAL COMMUNICATIONS.

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SOME OBSERVATIONS ON THE TREATMENT OF HAY-FEVER, WITH A REPORT OF 24 CASES TREATED WITH POLLEN SOLUTIONS AND 22 CASES TREATED BY THE ADMINISTRATION OF CALCIUM CHLORID.*

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There is a certain group of clinical symptoms to which a great variety of names has been given; names derived usually, from the real or apparent cause upon which the symptoms depend. Hay-fever, rose-fever, linden-fever, lacquer sickness, serum sickness, vaso-motor rhinitis, egg sensitization and so on, through a long list, are examples of this diversified nomenclature.

These symptoms in general are:

A. *Characteristic.* (Symptoms of one or more groups always present). 1. Itching, redness and oedematous swelling of the skin or mucous membranes, e.g. of the body, mouth, throat, nose, eyes, etc. (This includes miscellaneous skin symptoms, such as urticaria, eczema, herpes). 2. Sneezing, lachrymation, rhinorrhea. 3. Asthma (bronchial type), cough, glottic stenosis.

B. *Miscellaneous.* (Symptoms of one or more groups often present). 1. (General), Fever, malaise, chills, asthenia. 2. (Special), Vomiting, diarrhea, cardiac and respiratory disturbances, swelling of lymph nodes.

The number of substances already known to be capable of giving rise to this characteristic symptom-complex is very large. In the

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tables of Lübbert-Dunbar are given the names of more than fifty plants to the pollen of which some of their hay-fever subjects were sensitive. This list is now undoubtedly greatly enlarged by subsequent observations. To this we may add many fruits, such as strawberries, raspberries, pears, bananas, melons, etc.; vegetables, such as tomatoes, celery, spinach and other greens; fish; crustacea (lobsters, crabs); mussels (oysters); various worms, such as bothriocephalus, tænia, the common earth worm; insects, such as ephemeris; toads and frogs; eggs, milk, various meats, etc.

Now all these substances contain special protein bodies, and it has been shown with pollens, at least, that this protein is the active agent in causing the symptoms in question. A theory based on the presence of a hypothetical and specific proteolytic ferment in the sensitized body, has been proposed to explain the phenomena observed.

However, it is also a well-established fact that this same symptom-complex may be caused by a large number of substances which contain no protein whatever. Some of these substances are quinin, mercury, iodine, tannin, choral hydrate, sulphonal, ipecac, antipyrin, phenetidine, salol and other salicylates.

This fact cannot well be explained by the hypothesis relating to protein sensitization, but there would seem to be no logical reason why the vaso-motor mechanism concerned in the production of the sensitization-syndrome may not be set in operation in more than one manner, and when we are able to analyze the matter more fully, we may find some simple or more fundamental facts of physiological chemistry at the bottom of the whole series of phenomena.

The study of sensitization is the study of individuals, rather than of averages. There is something in the sensitized individual which has made his sensitization possible. For convenience, we call this a "disposition," or "tendency." Its obverse is "resistance" or "immunity" and we know this also as individual, specific and racial. At the present time, we are in no clear way to formulate any entirely satisfactory theory of sensitization. On the one hand, it appears to be closely related to what we know as anaphylaxis, although possessing what seem radical and essential differences: on the other hand, it touches, perhaps, alterations in the relations of the endocrine glands; in any case, it is probably a matter of body chemistry, and I believe that its explanation will eventually come less from clinical observation than from laboratory research.

It is the purpose of this communication to bring together a few observations relating to the treatment of that form of sensitization

known as "hay-fever" and to report one series of cases treated by the injections of pollen solutions and another series treated by means of the administration of calcium chlorid.

Treatment of hay-fever by specific protein de-sensitization. Except for desultory references, no report of this method of treatment appears in medical literature until the publication of the work of Noon and Freeman.¹⁻²⁻³ Following the stimulus of this work, numerous other observers⁴⁻⁵⁻⁶⁻⁷⁻⁸⁻⁹⁻¹⁰⁻¹¹ made trial of pollen solutions, and at present the method is being exploited by several manufacturers as a commercial enterprise.

TECHNIQUE.

Gathering the pollen. To gather a large amount of pollen is a laborious undertaking. I know of no better method than to place under the flowering plants, with their stems in water, glazed or other smooth paper, so as to catch the dropped pollen, which is very light, easily floating off into the air. The pollen which has fallen on the paper may be swept up with a camel's hair brush. By sifting the collected material through an extremely fine cloth sieve, it may be rid largely of insects and other extraneous matter. If thoroughly dried either in the air, or better, in a desiccator the pollen may be placed in a clean, dry bottle and will keep well at least for one year.

Preparing the pollen solutions. In preparing the pollen solution it is essential to select a method by which the active protein component may be extracted from the pollen as completely as possible, without loss of its active properties. It has been found by Kamman¹² that the active constituent of rye (and presumably of other pollen) is an albumin. It is therefore soluble in water, and under ordinary conditions in NaCl solutions.

Various methods have been proposed. Dunbar used alternate freezing and thawing. Clowes (l.c.) treated the dried pollen with acetone, and after evaporating to dryness, incubated with a NaCl solution. Kœssler (l.c.) adopted the following method: One centigramme of pollen is broken up as finely as possible in an agate mortar, and gradually 10 c.c. of an 8.5 per cent solution of NaCl is added drop by drop. This is then shaken for two hours and incubated at 37° for sixteen hours, centrifugalized, and the super-natant fluid removed with a pipette. Cooke's method (l.c.) is as follows: Dried pollen, or the polliniferous portion of the flower is ground in a mortar with sand, using a $n/200$ NaOH and 0.9 per cent NaCl solution. It is then shaken for twenty-four hours, filtered first through sand and then through a sterile Berkefeld filter. The nitrogen content of the solution is then determined by the Kjeldahl method. The

nitrogen content is the determining factor for the solution, doses being expressed in fractions of a milligramme of nitrogen.

In order to compare some of these methods, the writer made the following experiments:

Small quantities of mixed ragweed and goldenrod pollen were treated as follows:

- A. 1. Mixed with 5-10 c.c. of 0.5 per cent saline solution.
2. Moistened with a small amount of water and triturated in a porcelain mortar for fifteen minutes.
3. Treated with acetone, evaporated to dryness and 5-10 cc. of saline added.

All three samples were then incubated at 37° for 24-36 hours and examined under the microscope. The pollen grains in samples 1 and 3 appeared unchanged. Those in sample number 2 were largely broken up and disintegrated.

B. 1. 0.3290 gm. water-free pollen were treated with 1 c.c. acetone, evaporated to dryness, 30 c.c. saline solution added and incubated 24 hours.

2. 0.1814 gm. water-free pollen were ground dry in a Wedgewood mortar for one and one-half hours, 30 c.c. saline added and incubated 24 hours.

3. 0.330 gm. water-free pollen, 30 c.c. saline added and incubated 24 hours.

4. 0.476 gm. water-free pollen, 1 c.c. saline added and the whole frozen and thawed four times, then 29 c.c. saline added and incubated 24 hours.

These several solutions were then filtered through tared filters, washed thoroughly and the residues dried to constant weight. The results of these various methods were as follows:

Sample number 1 lost 21.2 per cent in weight.

Sample number 2 lost 33.9 per cent in weight.

Sample number 3 lost 24.9 per cent in weight.

Sample number 4 lost 25.6 per cent in weight.

As far as this single experiment goes, it appears that when the pollen grains are broken by trituration, a larger amount of soluble matter may be extracted by 24 hours' incubation than by any of the other methods tried. Moist trituration seems to be more effective than dry, and should be aided by the addition of sand or powdered glass. The amount of trituration necessary may be determined by the examination of a small portion of the ground material under the microscope.

Having ground a weighed portion of the dried pollen in an agate mortar with a small amount of water or saline solution, more salt solution is added and the whole incubated for 24 hours. At the end of this time, the mixture is centrifugalized at high speed and the clear super-natant fluid used as a basis for subsequent dilutions. If 0.025 gm. of dried pollen are taken and the final solution made up to 25 c.c. each cubic centimeter will contain the soluble matter in 0.001 gm. of dried pollen. From this, weaker solutions may be made by dilution as required. If the method of Cooke be employed, it is quite unimportant how complete the extraction has been made, or whether any fraction of the protein has been retained by the

Berkefeld filter, or lost in any step of the process, since it is only in the final solution that the determination of the contained nitrogen is made, and upon this finding the final dilutions are made. The method, however, requires more chemical training than most physicians possess.

Strength of solutions. Noon (l.c.) established the value of a unit of pollen solution as "the quantity of pollen toxin that can be extracted from the one-thousandth part of a milligramme of *Phleum* pollen." Clowes considered a unit as 0.000,000,05 gm. of pollen. Kœssler says "we understand as the unit of pollen toxin the 1-100th part of a millionth of a gramme of pollen proteid" although he writes it equal to 0.000,001 gm.

In general, it has been agreed that the unit devised by Noon shall be adopted; that the term "pollen unit" means the soluble protein contained in 0.000,001 gm. of dried pollen, and this is the value understood wherever the term is hereafter employed in this paper. It is a convenient quantity, and one into which the nitrogen value, if determined, may be easily translated.

Size of dose. No very definite uniformity exists as to the dosage of pollen solutions. Noon and Freeman advised giving for the first dose $\frac{1}{3}$ c.c. of the minimum dilution necessary to elicit the ophthalmic reaction; for the second and third doses, 50 per cent more than the first, and for the other doses, 100 per cent more than the first. Clowes gave 0.000,008 gm. for the first dose, and increased the dose by 50 per cent until a maximum of 0.000,025 gm. was reached. Lowdermilk gave 0.000,025 gm. for the first dose and increased it to 0.001 gm. Ulrich gave from 0.000,000,005 gm. to 0.000,001 gm. Kœssler gave for the first dose, one-half the quantity necessary to produce the ophthalmic reaction, and gradually increased the dose.

The attempt to determine the initial dose by means of the ophthalmic reaction is, in the experience of most observers, highly unsatisfactory, since, in the first place, to determine the minimum quantity necessary to produce the reaction is both laborious and uncertain, and further, granting that it could be determined with a limiting error of, say, 0.000,005 gm. of pollen solution, it would even then be quite unnecessary, as it can be shown clinically that arbitrarily to begin with one or two units is entirely safe, and vastly easier. As to the size of subsequent doses, this is to be determined by experience and by the facts observed in the individual patient under treatment. The sequence of doses used by the writer will be found in the case-reports given later.

Neither has the maximum dose to be given been definitely fixed. Several authors have selected 1000 units as the maximum. Others

are much below this quantity. At present, it seems as if any definite amount must be a purely arbitrary selection. I am convinced that in many, if not in all cases considerably more than 1000 units may be safely given after a sufficiently extended preliminary de-sensitization.

Frequency of dose. Injections of pollen solution are given variously at intervals of from one to ten days. No fixed rule has been established. It is considered unwise to give an injection during the continuance of what are called negative reactive symptoms due to a previous injection. Ordinarily, intervals of 3—5 days may be employed safely, and are in most common use.

THE TREATMENT OF HAY-FEVER BY MEANS OF CALCIUM CHLORID.

The initial inspiration to the use of calcium salts in the treatment of hay-fever seems to have been given by Wright¹³ who noted their value in relieving the urticaria due to the eating of fruit, and that arising from the use of diphtheria antitoxin. Chiari and H. Januschke¹⁴ noted the fact that in hay-fever and other rhinitides with abundant nasal secretion, calcium lactate $\frac{3}{4}$ gm. *pro die* relieved the symptoms. R. Hoffmann¹⁵ reported on the use of calcium salts in hay-fever and bronchial asthma having had favorable results. Kayser¹⁶ treated in 1912, one light case of hay asthma, and thirteen cases of typical bronchial asthma with calcium chlorid with good results, giving a 5 per cent solution. Emmerich and Loew¹⁷ reported five cases of hay-fever. All had taken CaCl_2 about 1.0 gm. t.i.d. for a long period of time, and all experienced almost complete relief from hay-fever symptoms. In a second communication, these authors¹⁸ state that the five patients cured by the use of calcium chlorid in 1913 had no return of the disease in 1914, having taken the drug more or less continuously in the interval. They report eight new cases similarly treated, and all were either entirely relieved, or had only the most trifling symptoms.

Dosage. The preparation and dosage are very simple. Calcium chlorid crystals, 100. Distilled water, enough to make 500. S. Take one teaspoonful in sufficient water, with or after each meal.

Patients have generally little or no difficulty in taking the drug as prescribed. There would seem to be no reason why it could not be made more palatable if desired. One of my patients complained of gastric distress and was obliged to reduce the size of the dose. Another complained of increased frequency of urination, and several of slight constipation. Patients having impaired kidney function might have to be watched, but in general there are no contraindications to its use.

Mode of action. That salts of calcium play an important part in body metabolism has long been known, although their exact functions are not altogether well determined. Emmerich and Loew claim that they (1) increase bodily energy, capacity and resistance; (2) relieve insomnia; (3) increase resistance against infection; (4) relieve tendency to nasal catarrh, laryngitis, bronchitis, etc.; (5) inhibit auto-intoxication. These claims do not appear to be justified by what is known of the physiological action of the drug, and must be considered to rest upon hardly more than an empirical opinion.

Lime salts have an important, if not essential, part in the activation of certain body ferments or pro-ferments, such as rennin, thrombin and trypsinogen. They are found also in the white blood corpuscles. There is a certain relationship between the parathyroids and the lime salts of the body. Hypo-parathyroidism is associated with lime deficiency, and tetany resulting from parathyroidectomy may be relieved by the administration of lime salts. This result, however, may also follow the administration of salts of the other alkaline earths, such as magnesium. It has been observed, both clinically and experimentally, that lime salts have a marked effect in lowering the irritability of the nervous system. (Sabbatini).

From such a survey as we can make of the relation of calcium salts to bodily processes, their influence upon hay-fever appears to admit of no very certain explanation based upon what is known as to the essential nature of the disease. Since, however, the clinical symptoms of this disease are dependent upon the mechanism of the vaso-motor system for their expression, and are due to an irritation of this system, it would seem probable that if calcium salts lower the irritability of nervous tissue, the benefits secured by their administration are due to this property, rather than to a more hypothetical influence upon the enzymotic activity of the body cells. At present, the role of specific proteolytic or other ferments in the production of hay-fever is largely hypothetical, however attractive the hypothesis, and to assume that calcium salts are of value in this disease in consequence of their action on cellular or other body ferments, is only to add one hypothesis to another.

During the past two years I have had a number of hay-fever patients under observation and treatment, the details of which are here given:

TREATMENT BY MEANS OF POLLEN SOLUTIONS.

Cases in 1914. Case I. C. B., age 22. Autumnal hay-fever many years with asthma. Ophthalmic reaction to mixed ragweed and

goldenrod pollen, markedly positive. Hypodermic injections of mixed pollen solution beginning July 25, as follows: 3, 8, 25, 70, 100, 200, 300, 300 units, two to five day intervals. Patient left the city for the East about September 1, and reported later by letter saying that he had had very little hay-fever at any time during the entire season.

Case 2. D. K. B., age 30. (See also 1915, case 31). Autumnal hay-fever nine years, no family history; some asthma. Ophthalmic reaction marked to mixed ragweed and goldenrod pollen. Treatment begun with mixed pollen solution beginning with three units July 28, and continued every two to four days until September 19, as follows: 3, 5, 15, 50, 100, 90, 150, 250, 200 (this dose was given August 19, and was made from freshly gathered ragweed pollen. It was followed by a marked reaction. There was much edema of the face and eyelids and some asthma, coming on within an hour after the injection and lasting twenty-four hours); 200, 275, 350, 400, 500, 500, (ophthalmic reaction still marked), 800, 800, 1000, 1000 units. Beginning August 17 the patient had slight hay-fever symptoms, gradually increasing in severity, but on the whole, experienced enough relief to be classed as "moderate improvement."

Case 3. C. S., age 14. Autumnal hay-fever seven years, very light for two years past. No family history. Ophthalmic reaction to mixed goldenrod and ragweed pollen positive. Treatment begun August 3 with three units and continued every three to five days as follows: 8, 20, 60, 80, 200 units. At this time (August 17) the patient was having hay fever symptoms rather worse than usual and discontinued treatment.

Case 4. Miss C. (See also 1915, case 20). Autumnal hay-fever fifteen years. Asthma until five years ago, none since. Had a light attack of hay fever last summer lasting about four weeks. Ophthalmic reaction to mixed ragweed and goldenrod pollen positive. Treatment begun with mixed pollen solution July 28. Ragweed alone was used in this and in the other cases treated during 1914, after August 19. Injections every 2—5 days as follows: 3, 6, 8, 25, 50, 100, 90, 150, 200, 200 (fresh ragweed pollen solution, followed by marked reaction coming on within 15 minutes after the injection. Ears felt hot and full; felt very ill as if she would die; eyelids very edematous; itching of palms and of skin generally; asthmatic attack; erythema on various parts of the body, particularly about the site of the injection), 100, 200, 300, 400, 500, 500, 800, 800, 800 units. The patient reported herself as having had almost no hay-fever after September 14, and as having been in general, 20 per cent better than usual.

Case 5. H. I. A., age 27. (See 1915, case 15). Autumnal hay-fever since infancy, with asthma, great-grandfather was a "sneez-er." Mother and one brother have hay-fever. Ophthalmic reaction to ragweed pollen, positive. Treatment begun July 28, injections at 2—3 day intervals; 3, 5, 20, 80, 125, 100, 150, 250, 200 (fresh pollen solution, followed by urticarial swelling of the arm, asthmatic attack and hay-fever symptoms), 100, 200, 200, 300 units. Patient left for Muskoka August 28, having had less hay-fever than usual up to that time.

Case 6. E. P., age 15. Autumnal hay-fever several years, not much asthma. Ophthalmic reaction ragweed, positive. Injections at 2—5 day intervals as follows: 2, 6, 20, 55, 100, 90, 150, 200, 200, 250, 300, 400, 500, 500 800 800 units. No reactions of moment. Hay-fever symptoms from August 17 were more moderate than usual.

Case 7. Dr. H. Autumnal hay-fever with occasional slight asthma for 15 to 20 years. Ophthalmic reaction ragweed positive. Treatment begun August 3 and continued every 2 to 5 days as follows: 3, 8, 65, 60, 150, 100, 200, 300, 400, 500, 500, 500 units. Patient left city September 4, reporting hay-fever symptoms to have been more moderate than usual.

Case 8. Dr. S., age 30. Autumnal hay-fever 15 to 20 years. Some asthma in 1909 and 1910. Had sub-mucous resection nasal septum operation April, 1912. Father has hay-fever, but for past few years only. No other sensitization known. Ophthalmic reaction ragweed, markedly positive. Treatment August 5 to September 4, as follows: 5, 14, 16, 30, 50, 100, 150, 200, 300, 300, 500, 650, 1000, 1000 units. September 4, ophthalmic reaction ragweed solution 1:100, positive. Patient had very moderate symptoms until first week in September, after which time, practically no symptoms at all. He said he "wondered almost, if there were any such disease as hay-fever."

Case 9. J. A. S., age 37. Autumnal hay-fever four years, becoming more acute each season. No family history. No asthma. Ophthalmic reaction ragweed, positive. Treatment August 14 to September 4 as follows: 25, 85, 100 (arm swollen about site of injection), 100, 200, 200, 300, 500 units. Asthmatic symptoms developed September 1 and became very troublesome. Hay-fever marked and distressing. In general, no improvement of symptoms.

Case 10. D. T. (See 1915, case 37). Age 27. Hay-fever several years. No asthma. No family history. Ophthalmic reaction ragweed, positive. Treatment August 27 to September 16 as follows:

20, 50, 100, 100, 200, 400 units. Patient reported in general, moderate improvement.

Case 11. D. P. R., age 41. (See 1915, case 17). Autumnal hay-fever many years. No family history. Ophthalmic reaction ragweed, positive. Treatment September 3-30, as follows: 25, 50, 100, 200, 300, 400 units. In general, symptoms slightly less marked than usual.

Five other patients were under treatment and either failed to report or left the city. For these, no report can be made.

Cases in 1915. Case 12. Mrs. E. S., age 35. Autumnal hay-fever nine years. Is dust-sensitive (road dust, house dust, etc.). Some flowers aggravate symptoms (carnations). Has severe hay-fever, with some asthma. No family history. Ophthalmic and cutaneous reactions to ragweed, positive. Cutaneous reaction, September 3, to pear, tomato, plum, celery, banana, all negative. Treatment, June 8 to August 25, 3 to 4 day intervals, as follows: 1, 2, 5 (arm sore and painful for 24 hours), 9, 20, 50 (erythema about site of injection), 80, 150, 300 (July 16, hay-fever symptoms for an hour or two, three days after injection), 450 (redness and swelling of arm after injection, also some hay-fever symptoms), 750, 850, 1000, 1000, 1000, 1000 units. August 17, sharp hay fever symptoms this morning, not related to injection. Patient placed on CaCl_2 , 1.0 gm. t.i.d. Hay-fever symptoms at intervals during the season, but on the whole, rather less severe than usual.

Case 14. W. S., age 33. Autumnal hay-fever 10 to 12 years. No asthma. Three brothers and one sister have hay-fever, and one brother died (anaphylaxis), after an injection of diphtheria anti-toxin. Ophthalmic and cutaneous reactions to ragweed, very positive. Cutaneous reaction, August 31 to pear +, cantelope +, plum —, peach —, banana —, apple —, horse serum —. Treatment, June 8 to August 24, as follows: 1, 2, 5, 8, 20, 50, 100, 200, 300, 500, 700, 850, 1000, 1000, 1000, 1000, 1000, 1000 units. August 24, hay-fever symptoms began developing as usual and patient was given CaCl_2 1.0 gm. t.i.d. September 14, hay-fever symptoms more or less marked. Reported later that symptoms continued during the season, possibly a little less severe than usual.

Case 15. H. I. A. (See 1914, case 5). Treatment (second year), June 9 to August 24, as follows: 2, 5, 10, 20, 50, 80, 125, 200 (slight asthmatic attack following injection), 300 (slight asthma), 450, 600 (marked asthma 15 to 30 minutes after injection, lasting 30 minutes), 700, 750, 850, 1000, 1000, 1000, 1000, 1000 units. August 24, left for Muskoka, having had no asthma (except that due to injections), and only the most trifling hay-fever symptoms.

Returned about the second week in September and had little or no hay-fever after this time.

Case 16. B. G. H., age 32. Autumnal hay-fever four years. One sister has hay-fever and is horse-sensitized. No asthma. No other known sensitization. Treatment, June 10 to September 4, as follows: 2, 5, 12, 30, 80, 300, 500, 700, 850, 1000, 1000, 1000, 1000, 1000, 1000 units. No report.

Case 47. D. P. R. (See 1914, case 11). Treatment (second year), June 2 to September 11. Cutaneous reaction, September 4, ragweed +, plum —, apple —, pear —, celery —, strawberry ++. Injections, 2, 5, 9, 25, 50, 100, 200, 300 (some hay-fever symptoms followed this injection), 600, 800, 1000, 1000, 1000, 1000, 1000 units. Patient out of the city in immune district August 14 to September 2. No hay-fever until his return, then symptoms developed with moderate severity, possibly, however, less than usual.

Case 18. Dr. A. A. G., age 45. Autumnal hay-fever 8 to 9 years. No asthma, but other symptoms severe. No family history. No other known sensitization. Ophthalmic reaction ragweed, very marked. Cutaneous reaction, August 31, ragweed +, pear —, plum —, banana —, cantelope —, peach —, apple, very faintly. Treatment, June 14 to September 11, as follows: 2, 5, 10, 25, 60, 125, 300, 500 (some local reaction), 700, 850, 1000, 1000, 1000, 1000 units. From about August 24 throughout the season, had more or less severe hay-fever symptoms, particularly after driving into the country, which he was obliged to do several times. On the whole, however, he thinks the symptoms were less severe than usual.

Case 19. H. R. B., age 26. Autumnal hay-fever since four years old. No family history. Knows of no other sensitization. Ophthalmic reaction ragweed, positive. Treatment by pollen injections, July 3 to August 28, then CaCl_2 , 1.0 gm. t.i.d. Pollen injections as follows: 2, 10, 40, 100, 200 (local reaction), 300, 600, 800, 1000, 1000, 1000, 1000, 1000 units. Hay-fever symptoms began August 17, and continued with moderate severity during the season. August 26, cutaneous reaction, plum +, cantelope +, celery +, ragweed +, strawberry +, (patient eats strawberries without trouble).

Case 20. Miss C. (See 1914, case 4). Treatment (second year), July 6 to September 6, as follows: 8, 15, 40, 100, 200, 400, 600, 800, 1000, 1000, 1000, 1000, 1000, 1000 units. Cutaneous reaction to tomato pollen, weakly positive. Patient was practically absolutely free from all hay-fever symptoms during the entire season.

Case 21. Mrs. C. B., age 37. Autumnal hay-fever since childhood. Slight asthma during the past two years. Cutaneous reaction ragweed +, pear +, plum +, tomato +, celery —, banana —. Treatment, July 17 to September 13, as follows: 6, 20, 30, 75 (slight local reaction), 150, 300, 600, 900, 1000, 1000, 1000, 1000, 1000, 1000, 1000, 1000 units. Slight hay-fever symptoms August 24 and throughout the season. Marked improvement. Less cough.

TREATMENT WITH CALCIUM CHLORID.

The following cases were treated exclusively with calcium chlorid, except that to a few patients who were having considerable ocular discomfort, a solution of epinephrin 1-10,000, was given for the transient relief which it afforded.

Case 22. Mrs. R., W., age 62. Autumnal hay-fever since seven years old. Attacks much less severe of late years than formerly, and apparently growing less each year. Almost no asthma. Of four children, the eldest son has hay-fever and asthma. A sister has vernal hay-fever. Cutaneous reaction ragweed, positive. Treatment, June 11 to September 18, CaCl_2 1.0 gm. t.i.d. September 11: during past four days some itching of nose, with coryza. Later, patient reports having had very little hay-fever, but thinks it has been about as usual.

Case 23. Miss M. T., age 21. Hay-fever since childhood, beginning in May and lasting until cold weather. Sensitive to flowers of all kinds, to dust, wind and smoke. Cannot sweep floors without marked discomfort. No asthma. Eye and nasal symptoms most marked. Has been using epinephrin solutions until they now only aggravate the trouble. July 2, lachrymation, coryza and sneezing of moderate severity, more or less continuously. Ophthalmic and cutaneous reaction ragweed (repeated tests) negative. Calcium chlorid, 1.0 gm. t.i.d. July 9, eyes "wonderfully better." Somewhat less sneezing and coryza. Less sensitive to dust and wind. July 20, much less uncomfortable than usual. On the whole, there is a marked amelioration of symptoms. July 28, very great relief. Is practically free from all symptoms. "I never was so helped by anything before." August 13, patient has no hay-fever symptoms whatever. The relief is absolute. September 6, absolute relief from all hay fever symptoms continues. October 27, has taken no medicine for past six or eight weeks, and has continued to experience absolute relief. Can sweep and dust, encounter smoke and wind without any symptoms of hay-fever.

Case 24. A. C. M., age 40. Autumnal hay-fever many years. Two brothers have hay-fever. Ophthalmic reaction ragweed, posi-

tive. Cutaneous reaction ragweed +, pear +, cantelope +, plum —, peach ++, banana —, apple, horse-serum —, strawberry —. Treatment, June 3 to October 1, CaCl_2 , 1.0 gm. t.i.d. No hay-fever symptoms of note until about September 5, then rather marked coryza and sneezing. Has taken several long railway journeys with only moderate discomfort. During the whole season, considerably less hay-fever than usual.

Case 25. L. K. M., age 44 (patient is brother of case 24). Autumnal hay-fever nine years. Two brothers have hay-fever. Asthma. No other known sensitization. Ophthalmic reaction ragweed, positive. Treatment, June 24 to about September 25, CaCl_2 , 1.0 gm. t.i.d. August 31, some asthma for past few days. During season, hay-fever moderate, possibly somewhat less than usual.

Case 26. Miss M. R., age 25. Autumnal hay-fever 7 to 8 years. No asthma. Maternal aunt has had hay-fever since childhood. Ophthalmic and cutaneous reaction ragweed, positive. (I was unable to elicit a positive ophthalmic reaction to ragweed in this patient in 1914). Treatment, June 11 to October 1, CaCl_2 , 1.0 gm. t.i.d. At first the drug seemed to cause gastric distress so that she could not take it regularly. Smaller doses than 1.0 gm. were necessary, with intermissions, for several weeks but the full dose was taken later. No hay-fever symptoms were experienced until September 5, when there was some sneezing and slight itching in the throat. At the close of the season she reported that she had had little or no hay-fever during the entire time.

Case 27. W. R. McL., age 27. Autumnal hay-fever ever since he can remember. No family history. Asthma doubtful. Patient thinks he has some idiopathy against peaches, plums and watermelons, the last named always making him hoarse. (Unfortunately it was impracticable to try the cutaneous test). Treatment, June 30 until some time in September. Patient reports, September 25, "I was much worse than usual."

Case 28. J. A. K., age 43. Autumnal hay-fever for 8 to 9 years. Slight asthma. No family history. Cutaneous reaction, ragweed +, peach —, plum —, muskmelon —, watermelon —. Treatment, August 28, CaCl_2 , 1.0 gm. t.i.d. The patient failed to take the medicine, and reported that he had experienced hay-fever symptoms of only moderate severity during the season.

Case 29. Dr. W. A. K., age 40. Autumnal hay-fever 15 years. Slight asthma lately. July 7, CaCl_2 , 1.0 gm. t.i.d. October 30 the patient reported that he had experienced only the most trifling hay-fever symptoms during the season.

Case 30. J. M. B., age 26. Autumnal hay-fever beginning for the first time last year. No family history. Last spring had marked attack of erythema on various parts of the body, which was thought to have been caused by eating strawberries. September 7, cutaneous reaction, ragweed +, apple —, strawberry (fresh fruit) —, CaCl_2 , 1.0 gm. t.i.d. During the month of September after returning here from immune district, had only moderate hay-fever symptoms.

Case 31. D. K. B. (See 1914, case 2). August 30, cutaneous reaction, ragweed +, banana, peach, plum, cantelope, apple, pear, all faintly positive. July 1, CaCl_2 1.0 gm. t.i.d. Slight hay-fever symptoms began about August 20, and continued, though rather less than usual during the season.

Case 32. E. F. H., age 25. Autumnal hay-fever since childhood, usually disappearing about September 10. August 26, cutaneous reaction ragweed +, peach ++, plum ++, muskmelon ++, celery ?, tomato +, strawberry +. CaCl_2 , 1.0 gm. t.i.d. Reported that during the season he had been slightly better than usual.

Case 33. F. P., age 43. Vernal hay-fever usually beginning about June 1 and lasting until end of July. June 12, is having about the usual amount of trouble at this time. Ophthalmic reaction ragweed, negative. Calcium chlorid, 1.0 gm. t.i.d., with almost immediate relief from hay-fever symptoms. Reports August 25, "I have been practically free from symptoms about half the time; the rest of the time, partly free and partly in trouble. About July 28 took a railway journey, traveling all day, weather dry and dusty, with no hay-fever symptoms whatever."

Case 34. B. D., age 26. Hay-fever since childhood, beginning in June and lasting all summer, with intervals of partial freedom from symptoms from middle of July to middle of August. August 25, cutaneous reaction, ragweed +, peach —, plum —, celery +, muskmelon +, watermelon +, tomato +, strawberry ++. (The patient has no knowledge of any ill effects from eating celery or melons). Calcium chlorid, 1.0 gm. t.i.d. September 7, asthmatic wheezing and troublesome cough about as usual. October 20, during the season hay-fever symptoms were much less than usual.

Case 35. Mrs. F. D., age 35. Autumnal hay-fever eight years. Has asthma badly at night, during the whole season. Sensitive to many flowers, also to dust. Strawberries cause pain, so that she does not eat them. Father had asthma. Cutaneous reaction, ragweed +, peach +, plum +, muskmelon +, watermelon —, celery +. Calcium chlorid, 1.0 gm. t.i.d. August 27, some asthma last night. Daughter, J. B., age 4 years, has been having hay fever symp-

toms for the past two or three days, for the first time in her life. (Cutaneous reaction, ragweed, positive, but not strongly, muskmelon negative). September 25, patient reported that she had been, on the whole, rather better than usual.

Case 36. Mrs. J. H., age 30. Autumnal hay fever nine years. No asthma. A son, age 6 years, has asthma of unknown origin. July 28, cutaneous and ophthalmic reactions, ragweed, very strongly positive. Calcium chlorid, 1.0 gm., t.i.d. August 3, has been having giant urticaria very badly for past week and has stopped eating fruit. Patient made no subsequent report.

Case 37. D. T. (See 1914, case 10), age 28. August 12, CaCl_2 , 1.0 gm., t.i.d. September 4, has been very comfortable as to hay-fever symptoms. Has been in the country, but suffered very little. Cutaneous reaction, ragweed +, tomato —, pear —, plum, faintly positive, apple —, banana —, strawberry, faintly positive.

Case 38. B. R., age 47. Hay-fever, autumnal type since 19 years old. No other known sensitization. Usually suffers most from August 20 to second week in September. August 6, ophthalmic and cutaneous reactions, ragweed +. Calcium chlorid, 1.0 gm., t.i.d. August 25, hay-fever moderately for two days. Cutaneous reaction, peach, faintly positive, pear +, cantelope +, apple +, plum +, banana —. Patient discontinued the calcium for a week in September, taking some proprietary compound from which she thought she had some relief. Then resumed the calcium. On the whole, the hay fever symptoms during the season were of only moderate severity.

Case 39. J. A. W., age 24. Autumnal hay-fever 14 years. No other known sensitization. No family history. No asthma. August 23, cutaneous reaction, ragweed, positive. Calcium chlorid, 1.0 gm., t.i.d. September 25, reports that he has had only moderate hay fever symptoms during the season. Has been better than usual.

Case 40. Mrs. R. A. J., age 47. Autumnal hay-fever with asthma eight years. About eight years ago, after eating celery, had a marked swelling of the mouth and face, with general itching of the body. A year afterward, had a similar experience. Since then, eating of celery has always produced a rather marked reaction: edema, urticaria and itching of the skin. September 1, cutaneous reaction, ragweed +, banana —, peach —, plum, faintly positive, celery +, pear —, tomato —, apple —, cantelope —. (All reactions more marked after an interval of an hour or two).

September 2, some further cutaneous tests were made as follows:
1. From the expressed and filtered celery juice, the reaction was

positive. 2. Alcohol in large volume was added to the expressed and filtered juice; the resulting precipitate washed with alcohol, then dissolved in saline solution and filtered. This final filtrate gave a positive reaction. 3. That portion of the alcohol precipitate insoluble in saline, also gave a positive reaction. (It is possible that this precipitate was not washed thoroughly enough to rid it of all traces of the precipitated albumin).

Calcium chlorid was prescribed t.i.d. September 25, reports marked relief from hay-fever symptoms after taking the calcium.

Case 41. L. F. M., age 20. Autumnal hay-fever fourteen years. No family history. Asthma marked. Some years ago was sensitive to celery, but is not so now. Has some difficulty with peaches, melons and plums. August 24, cutaneous reaction, ragweed +, watermelon +, muskmelon +, celery +, peach +, plum +. All cutaneous reactions were very marked and definite. Control tests were made with the same substances at this time with Drs. H. V. and W., all being absolutely negative. It is to be noted that the reaction to celery is positive, although the patient states that he is no longer sensitive to this substance, and can eat it without trouble. September 25, patient reports that he did not take the medicine prescribed (CaCl_2), but has suffered from hay-fever during the season, rather less than usual.

Case 42. F. W., age 28. Hay-fever beginning in August, for several years. Father has hay-fever. No asthma. Cutaneous, ophthalmic and nasal reactions to ragweed, negative. Cutaneous and nasal reactions to peaches, positive. Calcium chlorid, 2.0 gm. t.i.d. August 25, very comfortable. Has stopped eating peaches. Cutaneous reaction, peaches, negative. During rest of season, very little hay-fever.

Case 43. S. S., age 10. Hay-fever symptoms for three years. One attack of asthma three years ago. Mother has urticaria easily. Father thinks patient may be sensitive to melons. August 15, cutaneous and ophthalmic reactions, ragweed, positive. August 25, cutaneous reaction, peach +, plum +, celery +, muskmelon +, watermelon +, banana +. Calcium chlorid, 1.0 gm. t.i.d. Patient was fairly comfortable until early in September, when he left the city.

Case 44. C. S., age 25. Hay-fever for nine years, beginning in early spring and lasting until second week in October. Asthma. Symptoms marked. June 30, hay-fever symptoms distressing. Ophthalmic and cutaneous reactions to ragweed, negative. Calcium chlorid, 1.0 gm. t.i.d. Patient reported September 25. The hay-fever symptoms, which were severe, disappeared after the second

dose of the medicine, whereupon she promptly stopped taking it regularly. Afterward, took a long auto trip, without any symptoms. During the summer had occasional slight symptoms only, which disappeared promptly on taking one or two doses of the calcium. Has been practically free from all symptoms of hay-fever ever since beginning to take the drug. Thinks the results are "wonderful." She would probably have taken the calcium more regularly if it had not seemed to increase the secretion of urine and the necessary frequency of urination so much as to make her uncomfortable.

A number of other patients were seen and prescribed for, but failed to make any report.

THE RESULTS OF TREATMENT.

During the year 1914, sixteen patients were treated by means of injections of pollen solution. A few injections of mixed ragweed and goldenrod pollen were given, but ragweed pollen alone was used in most cases. Of this number, five discontinued treatment. The data for the eleven other patients are given in the following table:

Table I. Pollen Solution Injections, 1914.

Case No.	Number of Injections	Maximum No. Units Given	Duration Treatment	Results.
1	8	300	July 25—Sept. 10	+
2	20	1000	July 28—Sept. 19	+
3	5	200	Aug. 3—Aug. 17	—
4	20	800	July 28—Sept. 14	++
5	13	300	July 30—Aug. 28	+
6	18	800	July 30—Sept. 9	+
7	12	500	Aug. 3—Sept. 4	+
8	14	1000	Aug. 5—Sept. 4	++
9	8	500	Aug. 14—Sept. 4	0
10	7	400	Aug. 27—Sept. 16	+
11	6	400	Sept. 3—Sept. 30	0

Note. In this, and in the following tables, the signs used to record the results of treatment, have the following signification:

— Hay-fever symptoms worse than usual.

0 Hay-fever symptoms about as usual.

+ Hay-fever symptoms moderately relieved. Less than usual.

++ Marked relief from hay-fever symptoms. Very much better than usual.

+++ Either absolute freedom from hay-fever symptoms, or has only the most insignificant ones.

During the year 1915, the data on ten cases are as follows:

Table II. Treatment by Injection of Pollen Solutions, 1915.

Case No.	Number of Injections	Maximum No. Units Given	Duration Treatment	Results
12	18	1000	June 8—Aug. 25	+
13	21	1000	June 8—Sept. 6	+
14	18	1000	June 8—Aug. 24	0
15	20	1000	June 9—Aug. 24	+
16	16	1000	June 10—Sept. 4	—
17	16	1000	June 2—Sept. 11	+
18	15	1000	June 14—Sept. 11	+
19	13	1000	July 3—Aug. 28	+
20	14	1000	July 6—Sept. 6	+++
21	16	1000	July 17—Sept. 13	++

The treatment with calcium chlorid. Twenty-two patients were treated wholly or in part with calcium chlorid. The results and other data are given in table 3.

SUMMARY OF RESULTS.

In estimating the results secured by any method of treating hay-fever, we must remember the characteristic variability in the severity of symptoms which is so essentially and naturally a part of the picture of the disease. The symptoms in all pollen cases are, for one thing, in a direct ratio to the amount of the sensitizing pollen with which the patient is brought in contact. They are thus modified by weather conditions and local surroundings. It is also true that in a given individual there are seasonal differences in their intensity. What is true in pollen cases is undoubtedly true also in other forms of sensitization. For these reasons, the temporary cessation of symptoms, or slight differences in their severity must be considered as a part of the natural history of the disease. I believe it is fair to consider as modified by treatment, only those cases showing continued marked improvement, or at least a high average betterment, and those showing absolute, or nearly absolute, freedom from all symptoms. It is probable, or even certain, that this criterion rigidly applied, will exclude many cases which have really received benefit from treatment; but at least until our experience is more ample; it will be better to err in this direction.

Of the eleven patients treated in 1914 with pollen solutions, none were absolutely relieved, and only two could be said to have shown "marked improvement."

Of the ten patients treated with pollen solutions in 1915, one (her second year of treatment), had absolute relief, and one, marked improvement.

Table III. Treatment With Calcium Chlorid.

Case No.	Type of H.F.	Duration of Treatment	Am't CaCl. <i>pro. die.</i>	Result	Remarks.
22	A	Jun. 11—Sept. 18	3.0 gm.	0	Immediate improvement and absolute freedom from all symptoms after July 28.
23	V-A	Jul. 2—Oct. 1	"	+++	Multiple sensitization.
24	A	Jun. 11—Sept. 25	"	++	Multiple sterilization.
25	A	Jun. 21—Sept. 25	"	++	No symptoms until Sept. 25, then itching in throat with sneezing. No trouble afterward. Dose had to be omitted at times.
26	A	Jun. 11—Oct. 1	"	+++	
27	A	Jun. 30—Sept. 22	"	—	Sept. 25, patient writes, "I was worse than usual."
28	A	Aug. 28—.....	"	+	Patient did not take the medicine.
29	A	Jul. 27—Oct. 1	"	+++	Only insignificant symptoms.
30	A	Sept. 7—Sept. 24	"	+	
31	A	Jul. 10—Sept. 25	"	+	Multiple sensitization, faint.
32	A	Aug. 26—Sept. 25	"	+	Multiple sensitization.
33	V	Jun. 12—Aug. 1	"	+++	Immediate relief, and practical freedom from all symptoms about half the time.
34	V-A	Aug. 25—Oct. 1	"	+	Multiple sensitization, moderately marked relief during season.
35	A	Aug. 30—Sept. 25	"	+	Multiple sensitization.
36	A	Jul. 28—.....	"	+	No report.
37	A	Aug. 17—Sept. 20	"	++	Was in the country most of the time. Very little hay-fever.
38	A	Aug. 10—Sept. 7	"	++	Multiple sensitization.
39	A	Aug. 23—Sept. 22	"	++	
40	A	Sept. 2—Oct. 1	"	+++	Multiple sensitization.
41	A	Aug. 24—Sept. 22	"	+++	Did not take drug regularly.
42	A	Aug. 16—Sept. 22	6.0 gm.	+++	Ragweed reaction negative. Peach, positive. Stopped eating peaches.
43	A	Aug. 15—Sept.	"	+	Multiple sensitization. Left city.
44	V-A	Jun. 30—Oct.	"	+++	Multiple sensitization. Took drug irregularly. Relief immediate and complete. Ragweed reaction negative.

Of the four patients who were under treatment with pollen solutions and who received calcium chlorid as soon as their hay-fever symptoms developed, none were definitely benefited, even though they all reported themselves as being more comfortable than usual.

I am aware that as to pollen de-sensitization, these results do not appear to be as brilliant as those reported by other writers. Freeman reports 84 cases, of which 30.1 per cent were nearly or quite absolutely free from symptoms, and 34.5 per cent were greatly improved. Cooke reports 60 cases of vernal hay-fever with marked improvement in 60.5 per cent, and 80 cases of autumnal hay-fever with 25 per cent having marked improvement. Ulrich reports satisfactory results in about 60 per cent. Lowdermilk reports more than 70 per cent cured. Kœssler reports 41 patients, of whom 10 per cent were completely relieved, and 75 per cent markedly benefited. Oppenheimer and Gottlieb report on eleven cases with 45 per cent cured. Goodale reports on 79 cases, and is content with saying that about 25 per cent seemed to have received marked benefit from treatment.

In every case reported in this paper, either the ophthalmic or the cutaneous test, or both, was tried, and no patient was treated with ragweed solution who was not previously shown to be definitely ragweed sensitized. Further, all the pollen solutions were made by myself, so that their strength, quality and freshness were directly known.

To explain why the results I have obtained were less favorable than those of other observers, I am inclined to say that in part, this may be due to the fact that, for reasons already mentioned, I am unable to accept anything short of marked relief from hay-fever symptoms as definitely due to treatment, and even this degree of improvement, if it is more or less transitory, may arise from other causes.

Given a patient sensitized to ragweed only, his de-sensitization by means of ragweed pollen solutions appears to be a perfectly logical possibility; but from the fact that multiple sensitization can be shown to exist in so large a proportion of hay-fever subjects, the attempt to de-sensitize by means of the administration of any one sensitizing substance alone, would seem foredoomed to failure. I believe this fact may account for some of the failures in the treatment by means of pollen solutions.

The Cutaneous Test. The so-called cutaneous reaction was devised in Blackley¹⁹ in his experiments on the action of pollen, together with the ophthalmic and nasal tests. During the past sum-

Table IV. Cutaneous Tests.

Case No.	Rag-weed	Pear	Rach	Water-melon	Musk-melon	Ban-ana	Apple	Celery	Tomato	Straw-berry	Plum	Horse serum
12	+	-				-		-	-		-	
13	+	+	+		+	+	+		+		+	
14	+	+	-		+	-	-				+	-
17	+	-					-	-		±	-	
18	+	-	-		-	-	±				-	
19	+				+			+		-	+	
21	+	+				-		-	+		+	
24	+	+	±		+	-	-			-	+	-
25	+		-	-	-	-	-	-			-	
26	-							-		-	±	
28	+		-	-	-						-	
30	+						-			-	-	
31	+	±	±		±	±	±					
32	+	±	±		±			±	+	+	±	
34	+	-	-	+	+			+	+	±	-	
35	+	+	+	-	+			+			+	
45	+				-							
37	+	-				-	-		-	±	±	
38	+	+			+	-	+				+	
40	+	-			-	-	-				±	
41	+		+	+	+			+			+	
42	-											
43	+		+	+	+	+		+			+	
H.	-	-	-	-	-	-	-				-	
V.	-	-	-	-	-	-	-				-	
W.	-	-	-	-	-	-	-				-	
J.	-	-	-	-	-	-	-				-	
M.	-	-	-	-	-	-	-				-	

mer I have tried the cutaneous test in 22 hay-fever subjects and many normal persons, with a variety of substances other than pollen. All scarifications of the skin for the test were made under a magnifier with a needle point, in order to get them as nearly uniform as possible. Only the superficial and non-vascular layers of the skin were removed, so that commonly, no blood appeared in the abrasion. The results of these tests are shown in the following table.

The cutaneous test was made in these cases on the patient's forearm, although in persons prone to pigmentation of the skin it may better be made on some less conspicuous part. A sufficient number of minute abrasions made as above described, including one always for a control, a bit of the fresh fruit, pollen solution or a drop of

serum was either gently rubbed on the abrasion, or placed in contact with it for a few minutes; generally one to three minutes being sufficient time. The skin was then cleansed with a bit of moistened gauze, care being taken not to get a multiple inoculation at any spot. The control abrasion always showed a slight elevation of the skin immediately around it, and a small surrounding zone of hyperemia. The reaction was considered positive if there was a definite edema or wheal at the site of the inoculation. Where this edema, although measurably greater than that at the control abrasion, was nevertheless slight and rather transitory, the reaction was noted as +. A positive reaction was always accompanied by more or less marked hyperemia of the skin surrounding the inoculation, varying in degree with the intensity of the reaction. Other symptoms, such as smarting, burning and particularly itching, were frequently present. The reaction usually appeared in from three to five minutes, and lasted from half an hour to two or three hours.

Figure 1 shows the shape and relative size of the reactions occurring in case 41. In connection with the accompanying hyperemia, the picture was a rather striking one.

The materials chosen for these tests were chosen at random. If we will consider how extremely probable it is that a sensitized subject, such as case 41, would show a positive reaction against many other substances, the imperfect and partial character of the tests enumerated above will be better appreciated, and the enormous practical difficulties that may be encountered in attempts at specific de-sensitization. Not a few persons have been shown to be sensitized to such common articles of food as milk, butter, oatmeal, buckwheat; and if we add to these drugs, pollens, and protein substances generally, the list may be nearly endless (see Goodale, reference 6).

It is not my purpose at this time to discuss the cutaneous test at greater length, and the experiments which have been given are here introduced for the purpose of suggesting some of the difficulties which may lie in the way of the treatment of hay-fever by specific de-sensitization, whether by means of pollen solutions, or any other special sensitizing substances. It is possible, too, as already suggested, multiple sensitization may account for many failures in treatment with pollen solutions.

As far as my observations extend, although the number of observed cases is not large, the results of the treatment with calcium chlorid have been more satisfactory than those of treatment with pollen solutions. It must be noted also that none of the patients have taken the drug for that extended length of time which Em-

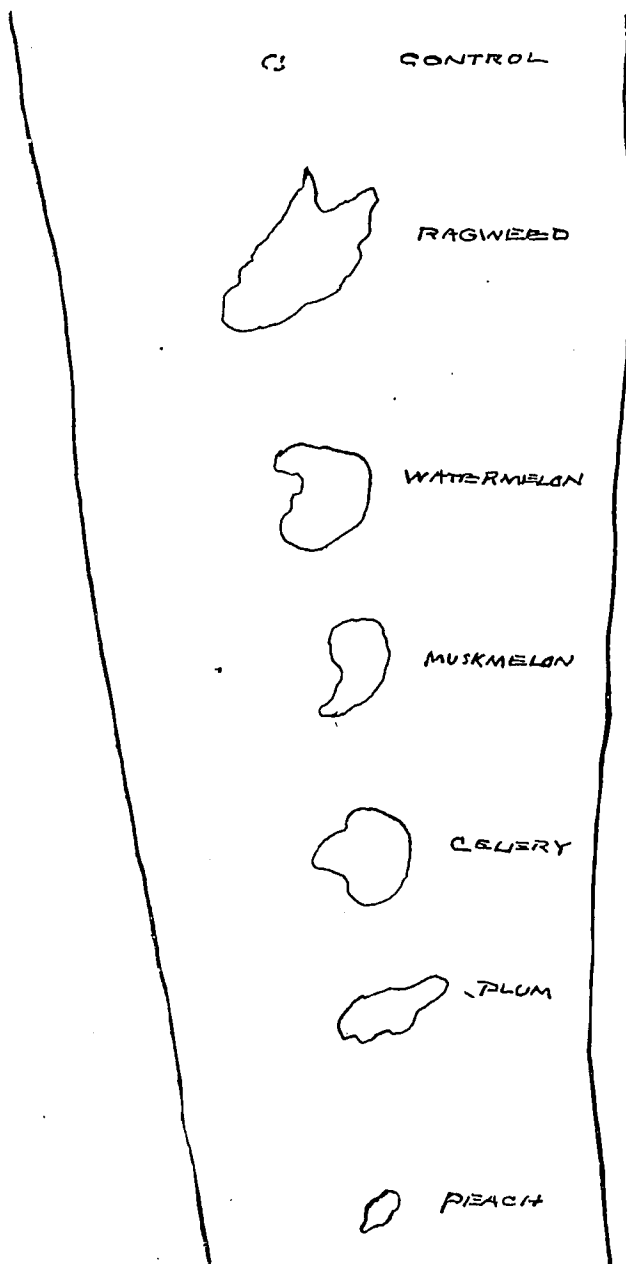


Figure 1. Skin Reactions in Case 41.

merich and Loew recommended. Although it has been shown that the maximum retention of calcium in the body occurs only after its prolonged ingestion, it may be found that its optimum effect may be secured with a less prolonged taking of the drug than has been advised. This may vary with individuals. Case 44 appeared to get almost immediate relief from 1.0 to 2.0 gms., and absolute immunity was brought about in case 26 within less than a month after beginning treatment.

There seem to be no definite contra-indications to the daily ingestion of 3.0 to 6.0 gms. of calcium chlorid. Anyone taking one or two pints of milk daily, will get as much calcium. If there is a tendency to constipation, it is easily remedied, while gastric distress may be overcome by a reduction in, or temporary discontinuance of, the drug.

Conclusions. 1. The de-sensitization of hay-fever patients by means of specific pollen solutions will materially relieve a small percentage of them if treatment is begun early enough. 2. Pollen solutions for therapeutic use should be prepared and used with great care and understanding. When improperly prepared or used, there is danger of serious, if not fatal, reactions. 3. Multiple sensitization is a frequent phenomenon in hay fever subjects, and its existence may account for many failures in the treatment by means of pollen solutions. 4. The treatment of hay fever by means of calcium salts rests largely on empirical observations, but from the limited data at hand, if the doses are sufficiently large, and prolonged through a more or less extended time, a large percentage of patients will receive material benefit. It is possible that vernal cases yield more readily than autumnal cases. 5. The administration of calcium salts is without danger to the patient and may be undertaken by any intelligent physician. It requires neither a careful laboratory technique, nor any special knowledge for its employment.

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Tuberculosis of the Superior Maxilla. RAFFAELE D'ALISE, *Annali di Odontologia*, Feb., 1916.

The author reports two cases which gave him the opportunity of carrying out some experimental studies. He states that primary tuberculosis of the oral cavity and especially of the upper jaw is rare. As regards the etiology and pathogenesis of tuberculosis of the jaws, he believes that dental decay and wounds resulting from teeth extractions open the way for the direct penetration of the tubercle bacillus, or the decay diminishes the resistance of the tissue and facilitates the localization of the tubercle bacillus in predisposed subjects.

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