of steel or iron should be near, when the test is being applied.

I wish to thank Prof. D. T. Cumstock of the Massachusetts Institute of Technology for a number of valuable suggestions concerning the use of magnetism for the above purposes.

BIBLIOGRAPHY.

- ¹ Smee, Alfred: *Med. Times*, 1844, p. 224.
- ² Aveling: *Proceedings, Med. Chirurg. Soc.*, 1851, p. 149.
- ³ Pooley, T. R.: *Archives of Ophthalmology*, 1880, p. 255.
- ⁴ Pooley, J. H.: *Gaillard's Med. Journal*, 1880, p. 357.
- ⁵ Kocher, T.: *Correspondenzbl. f. Schweiz. Aerzte*, 1884, p. 208.
- ⁶ Dumont: *Correspondenzbl. f. Schweiz. Aerzte*, 1884, p. 477.
- ⁷ Kälén: *Deutsche Zeitschr. f. Chirurgie*, 1887, Bd. 25, S. 82.
- ⁸ Graser: *Münchener med. Wochenschr.*, 1887, Vol. xxxiv, p. 273.
- ⁹ Kummer: *Rev. med. de la Suisse Rom.*, Genève, 1890, Vol. x, p. 646.
- ¹⁰ Lauenstein: *Deutsche med. Wochenschr.*, 1890, Vol. xvi, p. 551.
- ¹¹ Charon: *J. de Med. Chir. et Pharmacol. Brux.*, 1893, p. 42.
- ¹² Asmus: *Archives of Ophthalmol.*, 1894, p. 280; also *Klin. Monatsbl. f. Augenheilk.*, 1901, p. 423, and 1903, p. 262.
- ¹³ Gallemarts: *Bull. et. Mem. de la Soc. Franc. d'Ophthal.*, 1894, p. 143.
- ¹⁴ Hirschberg: *Centralbl. f. Augenheilk.*, 1890, p. 285.

Original Articles.

POLLEN THERAPY IN HAY FEVER.*

By J. L. GOODALE, M.D., BOSTON.

WITHIN a few years numerous reports have appeared in regard to the treatment of hay fever patients by the subcutaneous injection of pollen extracts. The writers, among whom may be mentioned Freeman, Noon, Cook, Clowes, Koesle, Manning, Oppenheimer and Gottlieb, have uniformly reported that a certain number of patients so treated have received more or less complete relief from the disease.

The object of the following paper is to report the results of observation based upon 123 cases of hay fever examined during the past 12 months with reference to determining if possible the value of this treatment, and also to ascertain what biological relations, if any, exist between the pollen of different plants.

In the first place, a word should be said in regard to the method of obtaining and preserving the pollen extracts. For many plants, which furnish an abundance of easily detached pollen, it is sufficient to gather the partly opened flowers, bring them into a room without currents of air, and in the course of a few days, the pollen may be shaken upon smooth paper. This applies particularly to those plants the cross fertilization of which is effected through the agency of air currents, such as many forest trees and grasses, and certain Compositae, particularly ragweed. In the entomophilous plants, where the cross fertilization is largely effected by the agency of insects, the freshly opened anthers may be clipped and gathered. The pollen is then either placed in the solution for extraction, or it may be preserved dry for an in-

definite period. I have taken pollen from specimens in my herbarium gathered 25 to 30 years ago, of grasses and of ragweed, which on the addition of water excites as marked a skin reaction as would be the case with freshly prepared extract.

The extract is obtained from the pollen by soaking in water for a few hours. I have not found it necessary to subject the material to trituration, as advised by some writers, and this is also theoretically unnecessary since the pollen grains in water promptly undergo a swelling, with solution of their albuminous contents. Several observers have complained of the difficulty of preserving the extract, and say that it is liable to deterioration on standing. After a number of tests, an alcohol dilution of 13 to 15% by volume seems to meet the requirements, and material prepared in this way a year ago has apparently lost little of its efficiency. It is interesting to observe in this connection that we have an example of a natural plant juice, namely wine, in which preservation of its qualities is thus secured. The heavier natural wines contain a considerable amount of albuminous matter, together with approximately 14% alcohol. More than this percentage checks the further development of the yeast plant, and this amount, while preventing decomposition, does not seem sufficient to cause a precipitation of the proteids of the wine.

It is desirable to keep the solution in amber bottles.

A word of caution should be said in regard to the gathering of flower heads for the preparation of pollen extract in the case of those plants which may contain a poisonous substance, as occurs in certain Compositae, especially the wormwood group. I have observed a few cases where disturbing symptoms of nausea and malaise followed the injection of such material to a greater extent than would be accounted for by the actual amount of pollen present. In the case, however, of such plants as the Rosaceae and grasses, these precautions are unnecessary and we may in the case of the latter, find it more convenient to strip off the flower heads or anthers by hand.

When the pollen has been gathered, and a suitable extract obtained, the latter constitutes then the stock solution from which varying dilutions are prepared. It is theoretically desirable to prepare the stock-solution with a definite percentage of pollen-extract, but with present laboratory methods this is difficult, and, moreover, it is not absolutely essential, since individuals differ very widely in their degrees of sensitization, and each case must be examined by different dilutions, to determine the correct strength which it is safe to use for the patient.

As has been described by other writers, and by a previous publication of mine, the tests are made by making a series of superficial scratches on the skin of the arm, and gently rubbing in a drop of the pollen extract to be tested into a scratch. After five to 15 minutes the positive re-

* Read before the American Laryngological Association, June 2, 1915, at Niagara Falls, Canada.

actions are indicated by varying degrees of local disturbance. These disturbances of the skin may be ranged in order of intensity as follows: In some cases the first perceptible alteration consists in a sharply circumscribed white area, not elevated, bordering the scratch for a distance of $\frac{1}{16}$ to $\frac{1}{8}$ of an inch. We may find in other individuals the first manifestation to consist of a slightly reddened raised area. In more pronounced disturbances the area of swelling is more extensive, and is more or less white in color, being surrounded by an area of reddening of varying size. When this degree of disturbance appears, it is usually accompanied by itching. It may, in marked cases, attain a considerable size, the edematous area reaching one inch or more in diameter and surrounded by half an inch or more of hyperemia.

The intensity of the skin reaction does not always seem to be proportionate to the clinical symptoms of hay fever. I have seen numerous severe cases where the skin reaction was much less than in other individuals who apparently suffered from a milder form of the disease. In the case of children the skin disturbances are relatively less pronounced than in the case of adults, and I have observed several under ten years of age, with apparently well-defined hay fever, who showed no reaction to the prevailing pollens borne in the air at the special season.

Examination of my cases by this method shows that the hay fever season in eastern North America may be divided into four periods as follows: The first period coincides with the flowering of the earliest blooming plants, the second with the flowering of the grasses, the third with the midseason flowers of July, and the fourth with the opening of the autumn blooming Compositae.

Of the first period 13 patients were observed who gave positive reactions to one or more of the following plants:

Coltsfoot (*Tussilago*)
 Dandelion (*Taraxacum*)
 White maple (*Acer dasycarpum*)
 Willow (*Salix nigra*)
 Alder (*Alnus incana*)
 Birch, white, yellow and black (*Betula papyrifera*, *lutea*, and *lenta*)
 Hawthorne (*Crataegus* sp.)
 Apple (*Pyrus malus* and *floribunda*)
 Lilac (*Syringa* var.)
 Oak (*Quercus rubra*)
 Tulip
 Lily of the Valley.

The symptoms which these early bloomers excite are relatively mild and depend chiefly upon the abundance of the plants in the vicinity of the patients. For many individuals the annoyance is so slight as to be perhaps not worth treating. In others a residence surrounded by maples or oaks, or with an orchard close at hand, may cause considerable discomfort. The most severe cases of this season which I have seen were

from maple and oak. If there is only one sensitization, the period of disturbance is brief and disappears with the drying or shedding of the flowers in question.

The second period represented by 36 cases, is ushered in with the flowering of the grasses. Owing to their abundance and the range of the blooming period of the different species, it is relatively severe and prolonged. Coincident with their flowering we may find an associated disturbance from many garden flowers, but for the majority of individuals, these latter are of minor importance. It is probable that if these June cases can be rendered immune to grasses, the other causes will be borne without much trouble.

The third period, represented by 10 cases, has been shown by my observations to be due in great measure to the mid-season Compositae, such as field daisy, hawkweed, yarrow, etc. With these are many species reported by patients which are still to be studied, such as chestnut, phlox, mountain laurel and numerous other plants of restricted distribution.

The fourth period with 77 cases begins with the general flowering of the ragweed, goldenrod, asters and the late Compositae and lasts until frost. My examination of the fields and roadsides at this season shows that the common plants other than the Compositae are relatively innocuous, and may be disregarded. Such are in the vicinity of Boston, the wild carrot (*Daucus carota*), pigweed (*chenopodium*), hardhack (*Spirea tomentosa*) and other representatives of these families.

From the foregoing observations it is evident that in this vicinity the chief causes of hay fever are the grasses and late Compositae. The early and midseason forms are briefer and less severe.

The possibility has been suggested that sensitization to proteids may arise through some paracutaneous entrance of the albumen in question into the body, and that hay fever, for instance, may originate from the contact of a given pollen with a scratch or abrasion of the skin. If this should be the case, it would certainly lay the method of testing by skin reaction open to serious objection, as we should thereby run the risk of exposing the individual to numerous sensitizations. I have gone over this point carefully with many patients testing them repeatedly with pollens to which they were originally negative, and have not, in any case, discovered the subsequent development of a sensitization.

METHOD OF TREATMENT.

The pollen extract is injected subcutaneously, and not into the muscles, as pain or stiffness may follow in the latter case.

The dosage is determined in the following way: After the special exciting pollen has been ascertained by the skin test, a second series of scratches is made at a distance from the first, and different dilutions of the pollen extract in

question are applied. It is important not to have this test applied in the vicinity of the skin which has been reddened by the first tests, as an increased excitability of this region is present, and even a simple scratch will cause localized swelling. The dilutions may be most conveniently made by adding a certain amount of the stock solution to alcohol of the same strength, and a 25%, 10%, 1% and even weaker dilution of the original extract are applied to the second series of scratches. The initial dose is determined by the dilution which fails to excite a definite skin reaction, and for the sake of causing as little smarting from the alcohol as possible, the quantity of material injected should not exceed five or ten drops. I should also recommend postponing the injection of even a small amount until after the reaction from the first skin tests have subsided, since a considerable amount of absorption from these probably takes place, and the introduction of an additional amount has seemed to me in a few cases to cause systemic disturbance. The injections may be made at intervals of two days to a week, increasing by a few drops at first, and later by the adoption of stronger percentages of the stock solution. To avoid the risk of anaphylactic disturbance, I have advanced the strength at first slowly. After five or more injections have been given, the strength may be increased with greater rapidity. The disturbances occasioned by the injection of the pollen extract below the skin consist, when a sufficient strength has been attained, of a more or less well-defined lump, varying from the size of a bean to that of a pigeon's egg, accompanied by a sensation of moderate heat and itching. It is interesting to note that none of the patients have complained of these manifestations as representing more than a trivial degree of discomfort, and in no case has the disturbance been sufficient to cause the patient to interrupt treatment.

Two instances of distinct but harmless anaphylactic shock were observed, one occurring in August in a man who came in somewhat exhausted from the heat, who showed extremely marked skin reactions, and who received on the same occasion a small dose of ragweed pollen extract. About half an hour after the administration of the pollen extract, he was taken with faintness, nausea and vomiting, and had to be assisted home. The other case was that of a boy who received a dose of grass and dandelion pollen insufficient to cause local skin reaction, but who, a few hours later, was taken with moderate prostration, nausea and vomiting. It has seemed to me consequently a wise precaution to make the initial dose approximately one-tenth of what the patient can theoretically receive with safety. After a number of injections have been given, it is practicable and safe to inject a strength which may cause distinct skin reaction, without exciting general disturbance.

Beyond the immediate anaphylactic shocks

above noted, I have seen in a few cases where ragweed pollen has been injected occasionally a more or less marked persistent general depression. Since using the pure pollen extract, such a condition has not occurred in my own practice, but it has been reported to me by patients treated by other physicians. It seems to me here to be a question whether there has been an injection of toxic material other than the pollen, or whether the dosage has been excessive.

RESULTS OF TREATMENT.

We have two methods of determining the effects that have been accomplished by the injection of pollen extracts, first, the behavior of the skin reactions; second, the patient's observations regarding his condition. The first phenomenon being objective in character should afford a more reliable guide as to what has been accomplished.

INFLUENCE OF TREATMENT UPON THE SKIN REACTIONS.

In those cases which it was possible to observe for a period of two weeks to several months, the skin reactions were carefully noted at regular intervals. Of these, 62 showed a distinct diminution in the size and intensity of the disturbances in the skin, two showed no appreciable change.

The time required for the diminution of the skin reaction varies within wide limits, dependent both upon the plant tested, and upon the individual himself. In the case of alder, willow and apple, I have sometimes obtained a marked reaction from the first application, but on repeating the application two days later, a diminution or total disappearance was noted. This sudden disappearance following the first scratch was noted also in a case of horse fever, which showed on one afternoon a very extensive swelling from the application of antitoxine to a scratch, but who on the following morning, tested with the same antitoxine, showed no reaction, and has shown none since. In the case of grasses, and even more in the case of ragweed, a slower disappearance of the reaction was noted. With ragweed and Cosmos particularly I have observed in some cases a persistence of the skin reaction, even after weekly injections carried on for a period of four to six months. In these more obstinate cases an increased tolerance, however, was noted in spite of the persistent swelling. This tolerance was shown by the disappearance of itching which the first injection had caused, and by the smaller amount of hyperemia surrounding the oedema.

Twenty-one cases of those whose reactions had diminished in the course of treatment were examined again after the lapse of two to six months. Of these 19 showed no return of the skin sensitiveness, and some of them showed a still further diminution. Three cases after the lapse of three months showed a distinct return toward their original degree of sensitization.

INFLUENCE OF TREATMENT UPON HAY FEVER SYMPTOMS.

In describing the results which have followed the injection of pollen extracts, it has seemed to me desirable to separate those cases which have received treatment during the hay fever season from those which have been treated during the winter or out of season. I have done this for the reason that it is difficult during the course of an attack to draw accurate deductions from the statements of the patients themselves. We have in the first place to remember that seasons vary in the severity of hay fever symptoms, dependent upon the amount of rain, heat and cold. Furthermore, the individual's predisposition seems to vary, perhaps as the result of his physical state and habits at the season. Finally the element of suggestion may conceivably play a part. While I shall therefore report the summer cases with reference to the degree of relief obtained, I do not regard these figures as at all conclusive. On the other hand, observations carried out during the winter with references to changes in the intensity of the skin reaction may be considered a fairly reliable guide, if it be admitted that the strength of the solutions themselves has not undergone deterioration. This latter point is difficult to determine with absolute certainty. Nevertheless, my alcoholic solutions seem now, after a lapse of months, to effect in new cases nearly, if not quite, the same degree of skin reaction, which they occasioned in a fresh state.

At the date of writing, 123 cases have been observed, of which 74 have had more or less treatment, 49 have been seen but once, or are now beginning treatment. Of the cases which may have been considered to have had a sufficient amount of treatment to enable us to draw more or less definite conclusions, 32 were treated after the onset of the hay fever symptoms, and 47 were treated during the winter or early spring. Of those cases which were treated at the beginning of the hay fever season, 26 expressed themselves as having been more or less relieved, eight could not see material improvement. In estimating the results actually achieved by treatment during the season I believe that an accurate judgment would place the extent of the relief in a number of instances distinctly below that which the patients expressed. It is possible that the element of suggestion plays here a considerable part.

Furthermore, a certain number of these who believed themselves improved showed but slight diminution in the extent of the skin reaction. It has seemed to me that such cases probably represent too high a degree of sensitization to obtain material relief during the hay fever season, and that a longer period of treatment is required. On the other hand, several of these individuals who reported several months later, showed a marked diminution in their skin reaction, and it was possible then to undertake their treat-

ment, with the result of bringing about still further a diminution in the intensity of the skin disturbances. About one-fourth, however, of those treated during the season experienced after a certain number of injections, ranging from four to 12 in number, such striking diminution in their subjective sensations and in the skin reactions that it seemed difficult to ascribe the gain to anything else than the treatment, the improvement noted having occurred from one to three weeks before the disappearance of their type of hay fever in this vicinity.

THE BIOLOGICAL RELATION BETWEEN DIFFERENT PLANT PROTEIDS OR POLLENS.

It is evident that in this work a knowledge of the biological relationships of the exciting plants would be of the greatest aid. If, for instance, we can say that the protein of two exciting plants is identical we shall need to inject the pollen of only one.

While we do not know clinically the relation of the different plant pollens, yet from a botanical standpoint, they have been studied by sero-biological methods by a number of observers.

The methods employed were the precipitation reaction and the agglutination method. Extracts of the plant albumen were made, removing first, where present, fats, oils, acids, alkalis, starches, glycogens and sugar. Those extracts were then injected into rabbits, preferably into the abdominal skin. As a rule the interval between injections was from three to four days.¹

With reference to the time required for immunization of the rabbits, no exact figures can be given. Sometimes a potent immune serum can be produced after three or four injections, but cases also occur where even after ten injections very little immunity had appeared—at times entirely failed to occur. Apparently the individuality of the animal is a factor. Uhlenhuth mentions that of ten rabbits injected with the same albumen, only one showed a potent immune serum. The test is done by removing a small amount of blood from the marginal vein of the rabbit's ear, adding a portion of the extract which was used for injection and centrifuging. If the serum is of high potency, a precipitate is shown. The animal is then separated from the others, not fed for 24 hours and then killed. The blood is received in sterile glasses from a carotid incision. The serum must be perfectly clear, and show no opalescence. Finally the serum must have no free antigen, that is, the animal must not be killed too early after the last injection. The serum, if absolutely sterile, is easily preserved in dark glasses and closed with sterile cotton.

Precipitation Method: Dilutions of the plant extract are made, beginning with 1 to 200 and ending with 1 to 50,000. To each of these dilutions

¹ Physiologische-systematische Untersuchungen über die Verwandtschaften der Angiospermen. Mez und Gohlke, Cohn's Beiträge zur Biologie der Pflanzen, 1913.

sible that the branch of the stem between the magnolias and Capparidaceae takes place above the mignonettes. Poppies do not act reciprocally with the mustard. The mignonettes, however, stand close to the violets. The Teasle family, Dipsaceae, which apparently resembles the Compositae, does not react with it, and we have here to do with an interesting case of convergence.

The accompanying diagram shows the mutual relationships of the families which have been studied by their serum reactions. Unfortunately the position of the grasses is not given in this diagram, as they belong to a separate trunk, namely the monocotyledons, but this fact renders it sufficiently evident that their albumen is wholly distinct from that of the dicotyledons. It has, however, been established that they are closely related in their reactions to the Liliaceae.

From the foregoing considerations it is evident that the families which chiefly concern us in this present connection, namely the Gramineae, the Compositae, the Rosaceae and certain families of trees, have no serobiological affinity with each other. Consequently an individual sensitized to one family alone would not react to the pollen of a distant group. Where two families are closely related as in the Rosaceae and Leguminosae, a positive reaction might be expected to both. The clinical evidence in this regard extends as yet only to the Gramineae and the Compositae. Clowes showed in 1913 that in individuals sensitized to both grasses and ragweed, immunization against the former conferred no immunity against the latter. Much consequently remains to be studied in this respect.

In the case of genera within a given family, a relationship of proteids has been shown to exist as already stated. We should therefore expect an individual suffering from ragweed sensitization to react positively also to goldenrod and to the other members of the Compositae. A case which reacts positively to beach grass would also react to June grass, red top, etc. A case reacting to roses would react to apples, cherries, Spirea, etc. We have, up to the present time, clinical confirmation of this view only in the case of grasses. Noon and Freeman showed that injection with one species of grass would also protect against other grasses studied. While they found the pollens identical, yet some grasses seemed to yield a more active extract than others, and in their later work used timothy grass by preference. My own study of the skin reactions in the case of grasses confirms this view, and, as I have previously reported, patients sensitized to one species react positively to others, although one may bloom in June and another *e. g.* beach grass, in August.

Sensitization to the Compositae represents for us in America the most important form of hay fever. This is sufficiently shown by the generally accepted opinion of the majority of sufferers, and is confirmed by my own statistics.

The question, however, has remained as yet unanswered whether among the Compositae themselves subdivisions exist of a serobiological nature. While we may admit a sufficiently definite affinity to cause positive precipitation or agglutination reactions among all its members, yet it is conceivable that the proteid of the Compositae may be still further differentiated in a manner corresponding to the different genera. Following the same hypothesis we may imagine an individual sensitized primarily to the golden rod proteid, who may show only in a relatively minor fashion sensitization to ragweed, with which he has perhaps never previously come in contact. He may consequently show marked reaction to the former and but slight reaction to the latter, yet in virtue of the underlying biological affinity of the two proteids immunization to the one may confer resistance also to the other.

During the year I have studied ten species of Compositae representing as many genera, in an effort to obtain light upon this subject. Two methods have been used, first the classification of patients with reference to their reactions or preponderance of intensity of their reactions to the pollen of these Compositae, second observation whether injection of one species of pollen would influence the skin reactions to other pollens.

1. Classification of Reactions.

A summary of the relative frequency of the various sensitizations is as follows:

Ragweed, 82 positive cases, 24 negative.

Golden Rod, 48 cases positive, 50 negative.

Cosmos, 28 cases positive, 25 negative.

Field Daisy, 28 cases positive, 37 negative.

Hawkweed, 20 cases positive, 39 negative.

Yarrow, 21 cases positive, 28 negative.

English Daisy, 16 cases positive, 19 negative.

Tansy, 11 cases positive, 20 negative.

Coltsfoot, 5 cases positive, 2 negative.

Dandelion, 6 cases positive, 1 negative.

The disparity between these figures immediately suggests the question whether the different test solutions contained proteids of different strength so that individuals with but slight sensitization did not react to certain weaker solutions, when they might have reacted to stronger ones. That this is not the case seems to be shown by the following table of 20 illustrative cases.

From this table it is evident that all manner of variations exist in the primary or preponderating sensitizations of individuals. I have been particularly struck by the difference in the grouping of reactions exhibited by patients coming to me from different localities. As yet sufficient data are not at hand to enable me to generalize in this respect, but experience so far has led me to expect a different display of reactions in a patient of my vicinity from that shown in a patient from western New York or from the middle West.

TABLE I.

CASES	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Ragweed	4	3	3	4	4	0	3	3	3	3	4	4	4	1	3	1	2	3	4	
Golden Rod	1	2	3	0	0	3	0	2	3	4	2	1	3	0	1	1	0	0	4	1
Cosmos	0	4	0	4	0	4	4	4	4	4	1	0	4	1	3	0	0	1		
Field Daisy	0	3	0	0	0	0	0	0	2	0	0	0	2	0	1	0	0	3	1	
Hawkweed	0	3	0	0	0	0	0	2	1	3	1	3	0	1	0	0	1	0		
Yarrow	0	0	0	0	0	0	2	0	1	1	2	2	0	1	0	0	3	0		
English daisy	2			3			2	1		1							3			
Tansy			0	0	0		2	1		2		4			0	0				
Coltsfoot	4									4										
Dandelion	4	4													3	1				

The intensity of the skin reactions is shown by the numerals:

0=Negative; 1=Slight; 2=Moderate; 3=Considerable; 4=Marked.

2. Influence of Treatment upon Reactions of Related Pollens.

The second method of determining the relations existing between the proteids in the related genera of the Compositae, has been by the following method. A patient who shows sensitization to, for instance, ragweed and goldenrod, is injected in the usual manner with ragweed pollen and observations are made at intervals with reference to the golden rod reaction. In some of these cases so studied it has been evident that with the diminution in the intensity of the ragweed reaction, there is a diminution likewise in the golden rod reaction, which, however, follows at some distance behind it, until the ragweed reaction has nearly or quite disappeared, when there is a sudden drop in the golden rod reaction. My observations in regard to this point are as yet incomplete and demand further study before they can be regarded as conclusive. There seems, however, here a promising field for study, and the method is suggested for the consideration of investigators who are entering upon this work.

If these observations are confirmed, they will serve to indicate that there are slight differences between related genera and yet a fundamental relationship.

From the theoretic point of view it would follow that while we may be able to accomplish immunization to all members of a given family by the injection of pollen from one, yet more rapid results may possibly be attained by em-

ploying a mixture of these pollens to which the individual shows preëminent sensitization.

The question may possibly be raised whether the parenteral administration of plant proteids may cause harmful alterations in the organs of the body. Longcope has shown that nephritis may be set up in animals by the subcutaneous injection of egg white. No examinations have been undertaken, so far as I know, on hay fever patients, as to whether the injection of pollen extract has been followed by the occurrence of albumen in the urine. I have made no examination of my hay fever patients in this regard. A case of horse asthma which I have reported elsewhere, received for a period of several months weekly subcutaneous injections of horse serum, in doses which finally reached the amount of five drops at each injection. The urine in this case was examined before and after treatment with negative results.

CONCLUSIONS.

Serobiological methods have shown the phylogenetic relationship of the different plant orders and families. The application of these discoveries to the treatment of hay fever by injection of plant proteids promises to assist in the selection of the specific material required for a given case.

Definite reactions are elicited in hay fever by the pollen of the exciting plants when brought into contact with an abrasion of the skin. The intensity of these skin manifestations may be sensibly diminished by the repeated parenteral administration of the proteids in question. Coincident with the diminution in the skin reactions, there seems to occur an increased tolerance of the exposed mucous membranes to the pollens of the plants employed. Pollen therapy in hay fever may be regarded at the present time as a promising method of treatment, but its value and the permanence of its results remain still to be definitely established.

REFERENCES.

- Freeman, J.: *Lancet*, April 25, 1914.
 Cooke, R. A.: *Laryngoscope*, Feb., 1915.
 Clowes: *Proc. Soc. Exper. Biol. and Med.*, Nov., 1914.
 Koessler: In *Forelheimers: Therapeutics of Internal Diseases*, 1914, Vol. 671.
 Gohlke: *Die Naturwissenschaften*, April 24, 1914.
 Goodale: *BOSTON MED. AND SURG. JOUR.*, Nov. 5, 1914.
 Goodale: *Ibid.*, May 20, 1915.
 Longcope: *Journal Exper. Med.*, Dec., 1913.
 Manning: *Journal Am. Med. Assn.*, Feb. 20, 1915.

LEPROSY AND ITS RELATION TO MASSACHUSETTS.*

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LEPROSY is not of such importance as tuberculosis to Massachusetts, but, nevertheless, is a problem which confronts us and which needs consideration and action. It is a disease of which

* Read at a meeting of the Boston Medical Library in conjunction with the medical section of the Suffolk District Medical Society, on March 31, 1915.