of chemically pure sulphuric acid in a test tube. The mixture is boiled over a flame and a standard solution of potassium permanganate added drop by drop while boiling until the solution becomes water white. It is diluted to 100 c. c. in Nessler jars, a standard solution of manganese sulfate added and Nesslerized. This method is so simple it can be carried out in twenty minutes. I have not used it myself of late except as a therapeutic guide.

I believe with Dr. McLester that with the 'phtalein test we do not have much trouble in making a diagnosis. These methods are of advantage in following our cases along therapeutic lines.

Dr. Gradwohl (closing).—In reference to the discussion of our Chairman, I wish to state that there is no question that every grave case of cardiac trouble has some renal impairment, and that every case of renal trouble has some cardiac impairment. I wish to be understood as making my remarks more from a laboratory man's standpoint than from the clinician's point of view. I am not responsible for the clinical examination of these patients, but this much I can say, and that is that after studying the earlier cases, those with only slight impairment, with only accumulations of uric acid, when my attention was called to the severe cases I found on investigation that none of the clinicians that I happened to know were able to make this differentiation; that is to say, this group of cases, as I have stated, was erroneously called "cardio-nephritis," and upon very close cross-examination on my part of these clinicians I was never able to get any one of them to state that this one is primarily a cardiac case or that one is primarily a renal case. In other words, they seemed to sidestep an exact clinical diagnosis. From my investigations I am satisfied that competent clinicians can not differentiate between these two conditions when they exist in an advanced state. Our results checked up by autopsies have shown that blood chemical methods have made such a differentiation. We, therefore, claim that blood chemical methods have succeeded where clinical or physical examination has failed.

We seem to have so much satisfaction with these methods in separating one group from another that I thought it was a matter of extreme importance to publish our findings and conclusions. Further than this, I wish to re-echo some of the remarks made by the Chairman (Dr. McLester) in his excellent address, that the methods of blood chemistry are not difficult; that any well-trained laboratory man can do them and their usefulness is almost beyond belief. I do not mean to say that every medical case observed should have a chemical analysis of the blood, but information is obtainable by these methods that I do not believe has ever been obtained in any other way. I feel that chemistry is coming into its own in connection with clinical medicine. I have always leaned to the side of bacteriology and serology in respect to their great importance in connection with the problems of clinical medicine, but I do believe biological chemistry is going to come to the forefront in the next few years in solving many of the difficult problems of everyday practice.

POLLINOSIS OR HAY-FEVER: ITS SPECIFIC TREATMENT

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INTRODUCTION

In 1819, Bostock, an Englishman, gave the first accurate clinical description of the disease under discussion. His analysis of the symptoms were so keen that later writers have been unable to add much of genuine importance. Bostock considered that the cause of the malady was to be sought in the emanations arising from hay, under the influence of the sun's rays, though the term "hay-fever" was in use prior to Bostock's time. Numerous theories came and went until the work of Charles H. Blackley made its appearance in 1873. A sufferer from the vernal form of the disease, Blackley chose to experiment upon himself in the hope of finding the true cause of hay-fever. In a series of remarkable, painstaking studies, covering a period of years, he gradually came to the conclusion that hay-fever is due to the pollen of certain plants. He devised wind plates for the detection of pollen granules in the air, showed that pollen is easily carried for long distances, and by means of inoculation tests demonstrated his ability to induce characteristic hay-fever symptoms at any period of the year. His work was partly ignored, partly overshadowed by the discoveries of Koch and Pasteur, until, in 1903, Dunbar confirmed and amplified Blackley's work, and firmly established the etiological significance of pollen in the production of hay-fever. Today no one doubts this truth—even though some contend that other factors assume an importance equal to that of pollen in the causation of the well known symptoms. Despite time-honored usage, therefore, the adoption of the term pollinosis in place of hay-fever would appear to be

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rational, since it conveys the definite notion as to the essential causative factor.

ESTABLISHED FACTS WITH REFERENCE TO
THE ETIOLOGY AND PREVALENCE
OF POLLINOSIS

It has long been recognized that two forms of pollinosis occur,—one in the spring from early May on, and one in late summer. Though clinically similar, they are caused by the pollens of totally dissimilar plants. Pollen granules are the male elements of flowering plants, and in themselves are incapable of reproduction. In none but so-called perfect flowers does self-fertilization occur; in all others it is brought about either through the agency of insects or of the wind. It has been pointed out, especially by Scheppegrell, that in the cases in which insects effect fertilization, the flowers in question are usually brightly colored or white, fragrant, possess honey glands, and produce relatively few pollen granules, as a result of which the plants in question assume little importance in the causation of pollinosis. On the other hand, plants fertilized by wind pollination are in most instances neither conspicuous nor fragrant, they possess no honey glands, and the pollen granules, which are very buoyant, are formed in immense quantities. Hence, for all practical purposes, only those pollens which are wind-borne need be considered active agents in the causation of pollinosis. As a result of these and other observations, notably those of Goodale of Boston, it has been possible to formulate the following conceptions:

1. Vernal pollinosis, often called "rose cold," is in most instances due to the pollen of some member of the Gramineæ or grasses. These are all monoecious plants. The pollen granules are unspiculated, and are presumed to cause irritation chiefly by reason of their high protein content. Studies seem to indicate that these pollens though very abundant are not carried very great distances by the wind. It has been estimated that in a timothy field during active pollination 8 million granules are given off for each square foot of surface. This group includes the grasses, both wild and cultivated, some cereals, such as rye, oats, and wheat, and possibly some trees, especially maples and oaks.

Timothy is perhaps the most frequent cause of this variety of pollinosis.

2. The autumnal form is due to the spiculated pollen granules of dioecious plants, belonging chiefly to the Compositæ family. About 85% of the cases in this part of the country are due to the pollen of the common or giant ragweed (*Ambrosia elatior* or *trifida*). Contrary to the general opinion, the pollen of goldenrod is not a frequent offender. Its pollen is toxic to susceptible individuals, but probably only by direct inhalation. Its pollen granules are relatively few in number and viscid, and insect fertilization is common, as is true of some other conspicuous members of this group, such as the daisy and asters. The reactions from these pollens are immediate, due to their abundant spicules, which vary from two to three microns in length. The granules possess a strong extine in contrast to the non-spiculated pollens and their protein content is low. The ragweed pollen possesses remarkable buoyancy, partly by reason of its small size, 380 million granules being required to make one gram.

3. Appropriate studies have revealed the significant fact that sensitiveness to one member of a group is usually associated with sensitiveness to all other members of the same group. This is evidence, therefore, in favor of the biological identity of the pollen proteins. It is valuable since it has led to the discovery that, in general, immunization with the protein of one pollen affords protection against the pollens of other members of the same botanical family. Immunization against ragweed, however, does not protect against goldenrod, according to Cooke.

4. The studies of Cooke and Vander Veer, upon human sensitization in general and hay-fever in particular, lead them to believe that "the sensitization is not directly inherited, although the tendency to spontaneous sensitization is inherited as a dominant character" in the Mendelian sense. Approximately 1 to 2% of the inhabitants of any locality, all of whom inhale the pollen, are sensitized. This one fact is essentially positive and conclusive evidence against the theory of a true "pollen toxin" in the Ehrlich sense of the word.

5. In the light of all available evidence we may, therefore, define pollinosis or hay-fever as a *seasonal state of anaphylaxis, occurring in individuals hypersensitive to the proteins of various pollens, with clinical manifestations usually limited to the mucous membranes of the eyes and respiratory tract*. Opinions differ as to whether "antibodies" actually occur in the blood of spontaneously hypersensitized individuals. Cooke and his co-workers have been unable to demonstrate them by any of the so-called immunity reactions. Inasmuch as many studies have tended to prove that the anaphylactic reaction is essentially cellular and not humoral, it is safe to assume, at present, that in pollinosis "antibodies" exist only in the sensitized tissues and that immunity in the true sense of the term is not conferred by present methods of treatment.

SPECIFIC THERAPY

It may be accepted as an established fact that pollinosis is not due to a true toxin, as was believed by Dunbar, who therefore attempted to treat the disease by passive immunization, using an "antitoxic serum" called "Pollantin" derived from immunized horses. Since the pioneer work of Noon in 1911 practically all specific treatment has been given along the lines of active immunization, quite analogous to the process of so-called desensitization in experimental anaphylaxis. The attempt is here made briefly to indicate the necessary data upon which appropriate treatment can be instituted.

1. *The Type and Degree of the Patient's Sensitization*—For this purpose it is necessary, first, to prepare *pollen extracts*. These should include the protein extracts of the common causative pollens of the vernal and autumnal types. Since the aqueous solutions are by no means of certain stability, even in the presence of cresol, it has seemed best to us to use the acetone precipitate method first introduced by Clowes. By this method one secures as a final product a fine powder quite readily soluble in water. The powder keeps indefinitely. The weight of the final product with relation to the weight of the original untreated pollen is used in the preparation of a so-called 1-500 solution. Such solutions form the basis for other

dilutions, and, if kept sterile and on ice, retain their potency for a month or more. Cooke makes his pollen protein dilutions in such a manner that they can be standardized in terms of milligrams of N per c. c. No matter how made, these solutions are employed in one of two ways.

(a) Intracutaneous tests, using .02 c. c. of 1-500 pollen dilutions, are carried out, in order to determine to what pollen or pollens the patient reacts. Positive tests usually come out quickly and are characterized by wheals of varying size and shape surrounded by a good erythema, often associated with local itching or even mild constitutional symptoms of hay-fever. The reactions persist for several hours, in some instances for a day, and may be accompanied by swelling of the arm. The local reaction is not necessarily a good index of the degree of sensitiveness.

(b) The Degree of Sensitization is next determined by means of conjunctival reactions. From the original 1-500 solution dilutions are prepared, with either sterile water or normal saline, of the following strengths:

1-1,000,000	1-50,000
1- 500,000	1-25,000
1- 250,000	1-10,000
1- 100,000	1- 5,000

One or two drops of the weakest dilution are instilled in the eye of the patient. At the end of five minutes, if no reaction has occurred, a drop of the next stronger solution is used, and one proceeds thus until a definite response is elicited. This is recognized by injection of the conjunctivæ and inner canuncle, lacrymation, and subjective symptoms of burning, often followed by sneezing and increased nasal secretion; in other words, the symptoms of pollinosis in a mild form. In case no reaction is elicited in a strength of 1-5,000, which represents a low sensitization, it is scarcely worth while to go ahead with the expectation of satisfactory results; in this case other pollens should be tried. The weakest dilution which elicits a definite eye reaction determines the initial dosage for that particular patient.

2. *Details of Treatment*—(a) The best results are secured when treatment is instituted about six weeks before the hay-fever season is due.

(b) The initial dose varies from .1 to .5 c. c. of the dilution just capable of producing a mild conjunctival reaction. The smaller doses are employed in highly sensitized patients; in general, in those reacting to dilutions of 1-100,000 or less.

(c) The injections are given subcutaneously and preferably in the same arm throughout: the injections usually cause a mild local reaction, with redness, possibly a little soreness, and, ultimately with the production of small painless bumps which may persist for some time after treatment is stopped. Under no circumstances should the injections be followed by constitutional reactions; if such occur, they indicate the use of too much or too strong a dose.

(d) Our experience has taught us not to increase the dosage by any rule of thumb. Each case is unto itself. The injections are given from once to three times a week, depending upon the original degree of sensitization. The aim of treatment is to reduce the sensitization to 1-1,000 or under, as measured by the conjunctival reaction, prior to the expected date of the onset of symptoms. The experience of the past year has shown that, in general, after the first three or four injections, one may give each time $\frac{1}{2}$ to 1 c. c. of a dose double that in strength of the one preceding. In several instances a dosage of 1 c. c. of a 1-50 dilution was reached before the season commenced. The decrease in conjunctival sensitiveness has been so consistent in our cases that we deem it unnecessary to make these tests oftener than once every two weeks. One must not be misled, moreover, by the occasional finding of "permanent conjunctival reactions." Just what is their explanation is not known; but, in the absence of constitutional symptoms, the injections of increasing strength should go on, regardless of a persistent eye reaction to weaker dilutions.

(e) Once the hay-fever season starts, treatment should continue as before; if high doses have already been reached, hold to this level and advance further if possible. If the dosage is still low, when pollen begins to be in the air and clinical symptoms become manifest, proceed with more caution, but according to the same rules.

(f) In case treatments are missed for a period of two weeks or over, commence all over as though the patient were being seen for the first time. Give not more than 1-10th of a c. c. of the dilution then found to cause an eye reaction.

3. *The Results of Treatment*—The published reports of Noon and Freeman, Clowes, Goodale, Ulrich, Oppenheimer, and of Cooke, have been singularly encouraging and remarkably uniform. The most extensive series is that of Cooke, who states that, in general, 75 % of the cases are relieved of 75 % are more of their symptoms and consequent discomfort. No one but a sufferer can truly appreciate what this really means. Our own experience has been most gratifying, for, with but one exception, all of our cases have experienced tremendous relief, amounting in not a few instances to a complete absence of symptoms while living under the same conditions as before. A number of points of importance are worth mentioning.

(a) In general, cases of ragweed pollinosis are more resistant than those of the vernal type.

(b) Patients showing the highest grade of sensitization give the most brilliant therapeutic results and seem to require less treatment to control their symptoms.

(c) In any case better results may be confidently expected with each successive year.

(d) The question as to permanent cure is of course a pertinent one. Probably the so-called immunity which is manifested by the clinical alleviation or absence of symptoms is slowly lost during the winter, the patient gradually returning to the sensitive state. This point, however, is not settled. There are undoubted instances of spontaneous cure. Our own work has led us to believe that even though complete and permanent desensitization may not occur, none the less each year's treatment effects a definite and permanent lowering of the patient's original reactivity. Improved methods of dosage and further immunological studies may show the way to secure permanent freedom from attacks.

(e) In cases of pollinosis complicated by asthma, the results are often most satisfactory, particularly when suitable studies reveal a blood calcium deficiency

which is adequately corrected. These conditions are most apt to be encountered in fat individuals showing polysensitization.

SUMMARY

Many points of practical and theoretical importance have necessarily been omitted from this paper. A great number of problems involved in the subjects of anaphylaxis and protein sensitization in general remain to be solved. Despite the incompleteness of our knowledge, we no longer need condemn the victim of pollinosis to six weeks of untold misery, or commend some long journey too often unsuccessful in its object. In active immunization with potent pollen extracts there is almost certain relief for the majority. In addition to this, of course, the patient's general health should be carefully watched, and all outspoken obstructive or infectious lesions of the nose, throat, or sinuses should be given appropriate treatment. Last, and by no means least, it is the duty of every progressive physician and citizen to work for the enactment of laws which will be effective in the ultimate eradication of weeds so needlessly the cause of intense suffering and great economic waste.
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TRICHOCEPHALUS DISPAR

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The object of this article is to draw the attention of those members of the medical profession who are interested in tropical medicine to the fallacy of the supposed non-pathogenicity of *Trichocephalus dispar* and also to stimulate the efforts of such men toward the discovery of an efficient remedy for the treatment of trichocephaliasis. A review of the literature on this subject leads the reader to believe that practically no symptoms, subjective nor objective, appear in trichocephalous infections, and probably on account of the little importance attached to its presence in the intestinal tract, no very careful and prolonged studies have been made with regard to its life cycle or the treatment of the disease.

In tropical countries where *Trichocephalus* is common other intestinal parasites are also common, and it is rather unusual in my experience to find *Ankylostoma*, *Lumbricoid*, *Strongyloid*, *Balanitidium coli*, etc., without also finding *Trichocephalus* present in the same patient. It is true, as claimed by all authors whom I have read on the subject, that one frequently encounters cases of pure infection of *Trichocephalus*, who apparently suffer no inconvenience from the presence of the parasites, and who show no signs nor symptoms of the disease, its presence being discovered only through routine examinations of feces; but the same thing may be said of nearly all the others, as any student of tropical medicine knows, and just why the pathogenicity of *Trichocephalus* has been overlooked by otherwise careful observers is hard to explain with any degree of surety, but probably the severe symptoms of *Trichocephalus* have, in many cases, been attributed to other parasites coincident with *Trichocephalus*.

So far as the writer has observed, the symptoms and signs of trichocephaliasis are practically identical with those of ankylostomiasis, the only difference being that of degree of severity, that is, I have seen *Ankylostoma* (and also *Lumbricoid*) cases that showed a little more severe toxemia, anemia, and concomitant symptoms than the worst cases of trichocephaliasis I have encountered; but to say that trichocephaliasis does not cause severe symptoms such as toxemia and anemia is a fallacy and the subject should be studied more carefully with the object in view of learning definitely the life cycle of the parasite and discovering some efficient means of expelling it from the intestinal tract.

In this connection it would seem appropriate to cite just a few cases in order that the reader may decide in his own mind whether or not the writer is correct in his assumptions.

CASE REPORTS

Case 1.—Mercedes O., white child of Spanish parentage, born in Cuba, eight years of age. Very anemic and listless; fairly well nourished, but muscles flabby. Although coming from ordinarily intelligent parentage, the patient is dull and does poorly in school, becomes easily fatigued and does not show the ordinary interest in what