With the Author's Compts.

NEW OBSERVATIONS ON HAY-FEVER,

WITH

NEW EXPERIMENTS ON THE QUANTITY OF OZONE IN THE ATMOSPHERE.

BY

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Mr. President and Gentlemen.—As most of you will be aware, I have for some years been investigating the phenomena and causes of hay-fever, a disease from which I myself suffer. At the time my work was published in 1873 * there were some points that remained unsettled, and it is only recently that I have been able to finish my investigations on these points. I propose this evening, therefore, to show you some of the instruments and the methods I have used, and more particularly to bring under your notice the results of experiments made with one or two instruments not described in my work. In order to make my observations intelligible to those who are not acquainted with what has been already published it will be necessary to sketch rapidly the course hitherto pursued. To such experiments therefore as have been previously described I shall only briefly allude, but to such as may be new to you I shall devote as much time as we have at our disposal.

When my investigations commenced in 1859 all was obscure and uncertain, and I had to tread my steps slowly and carefully. Bostock, who was the first writer on hay-fever, believed heat to be the cause of his attacks, and I for a time believed mine to be due to the same cause. The fact that dust seemed to bring on attacks was the first circumstance that made me to doubt, and when it was noticed that dust had this effect only at one time of the

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* Experimental researches on the Causes and Nature of Hay-fever. London: Baillière, Tindall, and Cox, 1873.

year I felt that the subject would need a careful investigation. A microscopical examination showed that dust contained pollen, but as it also contained other organic bodies pollen might or might not be the cause of hay-fever.

In 1859 I was brought accidentally into contact with pollen in a way that precluded the possibility of the attack which followed being due to any other cause. Many experiments were subsequently tried and almost invariably ended in bringing on attacks of sneezing and coryza when pollen was applied to the mucous membrane of the nares, and in all my experiments on the effects of dust it was found that when pollen was absent there were no symptoms of hay-fever produced.

At this time and for some years later I believed that I was the first to discover the principal cause of hay-fever, but I found subsequently that Elliotson had in 1831 * intimated that pollen might probably be found to be the actual cause of the malady; he had not, however, proved it to be so.

In addition to heat, pollen and dust, other agents, such as light, coumarin, benzoic acid, odours of various kinds, and also ozone, had been supposed to bring on the disorder. It was therefore necessary to put each of these agents to the test of experiment before we could be sure that pollen was the sole or even the principal cause of the ailment. The influence of heat was soon determined. It was only necessary to note the changes of temperature in the atmosphere during and after the prevalence of hay-fever to prove that these did not run parallel with the changes in the intensity of the symptoms of the malady and could not therefore be a cause. Precisely the same thing may be said of light.

Benzoic acid volatilizes only at temperatures much higher than any we ever have in the atmosphere and why it should have been thought of as a cause of hay-fever I cannot understand. Coumarin, the odoriferous principle of the *Anthoxanthum odoratum*, (one of the meadow grasses) is a volatile body of a very penetrating odour, and may well have been thought to produce hay-fever, but neither this

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* London: 'Medical Gazette,' vol. viii, 1831, pp. 411—13.

nor any of the other odoriferous substances experimented upon would bring on the disorder with me.

Schönbein had stated that atmospheric ozone seemed at times to bring on catarrh and the inference drawn by some writers on hay-fever was that ozone might be a cause of the malady. In order to determine this test papers (Schönbein's), procured from one of the London dealers, were exposed at the sea-side, but when half-a-dozen slips were exposed together, the depth of colour was never the same in all.* A second lot of test paper, made on Schönbein's method under my own superintendence, was better, but was by no means perfect, and it occurred to me that I would try the effect of covering one surface of the paper with unboiled starch and solution of potassium iodide.† This plan answered much better, but on account of the difficulty of covering the paper evenly it did not meet all my requirements.

Strolling one day by the sea-side during one of my summer holidays I noticed what is often seen on the sea shore, namely, a stretch of sand that had been left by the receding tide as smooth and flat as it would have been if trowelled by a careful and skilful hand. The idea at once struck me that if water would deposit grains of sand in this manner it might be made to deposit granules of starch in the same way. On my return home I had a very simple apparatus ‡ constructed by means of which I was enabled to deposit a thin layer of starch on one surface of a sheet of blotting paper.

This plan answered admirably. In the evenness and smoothness of the surface it gave it far excelled the work of the most skilful hand. The surface is a pure white and so delicate is the power of adjustment by this method that the quantity of material laid upon a given area, say of half an

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* From a communication I had from the late Dr. Daubeny, it would appear he had had a similar experience.

† Schönbein's paper is soaked in *boiled* starch and solution of potassium iodide.

‡ This consists of a thin frame of brass with a frame of wood attached to it to strengthen it. The mode of using this, the formula for the starch mixture, the plan followed in constructing a scale, and also the quantity of iodine liberated at the various points of the scale, I hope to be able to give in another place.

inch square, can be regulated to the $\frac{1}{1000}$th of a grain. The surface presented to the atmosphere has also the important advantage of being composed only of the two substances to be acted upon, namely, the starch and the potassium iodide. When acted upon by ozone, unlike Schönbein's or Moffat's paper, the colour produced varies from the palest yellow to a deep cinnamon brown or even a brownish black.

I had now a test paper that answered well the objects I had in view, namely, 1st. To determine in what ratio the quantity of ozone increased in ascending a given scale, and 2nd. To ascertain what relative quantity of this body would have to be inhaled to bring on catarrh if it was found to have the power to do so.

You are aware that in this test the ozone liberates the iodine from its combination with potassium and permits the former body to act upon the starch and thus to produce the characteristic colour. Free iodine operates in a similar manner but acts directly upon the starch.

The simple instrument shown in Fig, 1* exhibits this mode of action and it is by the use of this apparatus that I have been able to form some notion of the relative quantity of ozone at various points of a given scale. To the use of this instrument I shall refer again presently.

By experiments at the sea-side it was found that the quantity of ozone needed to produce each succeeding degree of a given scale increased in a somewhat rapid ratio, and that to produce the deepest tint on a scale of thirty degrees it would require from five to six hundred times the amount of ozone necessary to produce the lowest degree. Ozone is seldom present, even at the sea side, in this large quantity, but is often found in quantity sufficient to produce the middle tints, and these require from two to three hundred times as much as suffices to produce the lowest degree. Even in the largest quantity, however, ozone did not at any time bring on hay-fever and two of our most experienced meteorologists tell me they have never known it to bring

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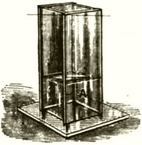
***** The instrument exhibited when this paper was read was more elaborate than that shown in Fig. 1. This is, however, much more simple and is easily worked, whilst it is at the same time more reliable.

on catarrh. Moreover, when we consider that the spot where ozone is most abundant is the place where hay-fever patients are most free from their ailment, we cannot but wonder that this substance should ever have been thought to bring on the malady. There are, however, one or two other points to which I wish to draw attention and which together form the chief reason for my having gone somewhat into detail on this question of the action of ozone.

We have seen that ozone does not seem to bring on catarrh or hay-fever, but if ever it should be proved to do so it must be by the inhalation of exceedingly small quantities. The amount in the atmosphere necessary to develope those tints which correspond to the quantity which was thought by Schönbein to bring on catarrh are, as I shall be able to show, very small. But a much more important consideration arises from the circumstance that it is almost universally believed that an atmosphere in which ozone is moderately abundant is one that is favorable to health. I shall I think be able to show also in this case that so far as this health-giving property is dependent upon the presence of ozone it must in most instances be an exceedingly small quantity of the active agent that produces this condition.

I have said above that free iodine acts upon the test paper somewhat in the same manner as the iodine liberated by ozone, and that the instrument shown in fig. 1 exhibits this mode of action. Iodine dissolves freely in proof spirit, but pure water has the property of giving up rapidly a

FIG. 1.



A. A square glass tube formed of four slips of glass, two inches long, cemented together, and to the foot-piece by Canada balsam. The opening of the tube is exactly half an inch square.

large portion of its iodine when a minute quantity of the alcoholic solution is placed in a small quantity of water.*

In using this apparatus we take advantage of the above-named circumstance. Ten grains of distilled water are placed in the tube, as shown at A, and to these are added one grain (by measure) of an alcoholic solution of iodine, which contains one grain in one thousand. This mixture is allowed to stand until it gives no perceptible tinge of colour to a piece of the test paper when placed over the opening of the tube and covered with a slip of glass for twelve hours. If we now add one grain of the same alcoholic solution of iodine and keep the opening of the tube covered with a slip of the test paper until the iodine is exhausted we shall find the paper coloured a deep cinnamon brown. We can now determine with tolerable accuracy the quantity of air that is necessary to be brought into contact with the surface of a piece of test-paper in order to liberate sufficient iodine to colour the paper up to the point attained by the expenditure of ·001 of a grain of iodine. In a brisk wind the air travels at the rate of rather more than twelve miles an hour, but if we take it as moving at the rate of ten miles per hour for a period of twelve hours, 1,900,800 cubic inches of air will pass over a square half inch of test-paper set with its face to the wind for the time named. Dr. E. Smith calculated that a hard-working labouring man would in twenty-four hours pass into and out of the lungs 1,568,390 cubic inches of air, whilst an ordinary adult in a state of rest would only take in 686,000 cubic inches. If we take the average consumption to be 1,000,000 cubic inches in twenty-four hours, it would take nearly forty-eight hours for an adult to inhale as much ozone as would liberate ·001 of a grain of iodine from its combination with the potassium. It is, however, highly probable that only a certain proportion of the ozone is absorbed from the air which passes over the test-paper, but if we allow *nine tenths* for waste it would still be necessary for an adult to inhale

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* Possibly some portion of the iodine is converted into hydriodic acid also. The alcoholic solution will evaporate and colour the test, but is not so regular in its action when used alone.

for nearly five hours, in order to take in as much ozone as would suffice to liberate the weight of iodine named. Even at the sea-side it rarely happens that an exposure of twelve hours will give the depth of colour obtained by the expenditure of ·001 of a grain of iodine. The average will probably be not much more than one fifth of this quantity.

In some situations the quantity of ozone present in the air is excessively small, only the faintest tinge of colour being seen after a prolonged exposure of the test. By following a similar method of experimentation to that detailed above, we can form some notion of the exceeding minuteness of the quantity of ozone that produces this change in the test-paper at the lowest points of the scale.

As in the former case we first place ten grains of distilled water in the tube (fig. 1). To this we add one fourth of a grain of the alcoholic solution of iodine* (one grain in one thousand), and allow this to stand until it gives no perceptible tinge of colour to a slip of test-paper placed over the opening of the tube for twelve hours. We now add one quarter of a grain of an iodine solution, which contains one grain in 5000. If we cover the opening of the tube with a piece of test-paper for twelve hours, a delicate pale yellow tint is produced, the expenditure of iodine being ·00005 of a grain.† When we take into account the fact that two million cubic inches of air will sometimes pass over the test-paper in bringing about this change we shall be able to form some idea of the excessive minuteness of the quantity of ozone in the atmosphere, but which is yet capable of being detected.

It is, however, possible for ozone to be present, and yet to escape detection in the ordinary method of using the test. If we expose a slip of paper when the amount of ozone in the air is very small, a considerable time will elapse before any change of colour is perceived, and if this

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* This may easily be done, without the trouble of weighing, by using the instrument shown at fig. 7.

† By operating with a tube of very small diameter, say the $\frac{1}{80}$th of an inch, it is not difficult to show the reaction of so small a quantity as the $\frac{1}{100000000}$th of a grain of iodine.

time should go beyond the usual period of exposure, it will seem as if no ozone were present. But this want of action is often only apparent and not real. This may be demonstrated in the following manner. A slip of test-paper is exposed, so that one third of its surface is covered from the wind; at the end of a given time and before any tinge of colour is seen the slip is moved, so that the covered part is exposed and one half the other portion is covered. It is now exposed for the same length of time as before, and if ozone is present the middle portion of the test will show a change of colour, whilst the two ends remain unchanged. In this way an undercurrent of unperceived action may go

FIG. 2.

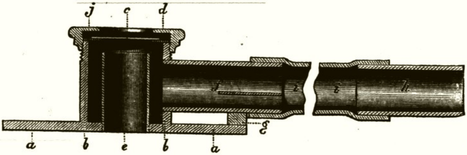

FIG. 2.—A perpendicular section of the instrument represented. *a, a*, brass plate to which the brass cylinder *b, b* is soldered; *c*, a square of thin microscopic glass, on which a cell one centimètre square is made with black varnish; *d*, a loose cap, which screws on to the cylinder *b, b*. When screwed down, the under and inner surface of this cap rests on small pins, which surround the square of thin glass. *e*, a smaller cylinder, which is made to screw into the plate *a, a*; *f*, a brass or glass tube cemented or screwed into the cylinder *b, b*; *g*, brass step screwed to the plate, *a, a*, the tube *f* being cemented into a semicircular recess on the upper surface of *g*; *h*, a short length of glass tube to be used as a mouthpiece; *i, i*, caoutchouc tube attached by one extremity to the tube *f*, and by the other to the mouth-piece *h*. This tube should be sufficiently long to reach the mouth of the operator when the instrument is placed in position on the stage of the microscope, and the eye of the operator is in position at the eye-piece. A slip of thin glass is shown to be inserted in the tube *f*; *j*, a disc of thin brass perforated, with a square opening rather larger than the cell on the thin glass. This disc is made to rest upon the upper edge of the cylinder *b, b*.

Drawn to a scale of ⅔rds.

on for any length of time. What part this kind of action may, in this case, play in the economy of nature it is impossible now to say; nor yet is it possible at the present time to determine how far it prevails in other departments of nature. It is, however, probable that in some it plays a very important part.

It had been shown that pollen would bring on some of the symptoms of hay-fever, but it was not certain that the yearly attacks were caused by pollen in the atmosphere. To determine this various methods of experimentation were tried. Several different forms of aspirators were used; one of these is shown in figs. 2, 3, and 4. If, whilst the instrument is on the stage of the microscope, the operator inhale through the mouthpiece *h*, whilst the thin glass is kept in focus, the solid matter in the air will be seen to deposit itself on the under surface of the glass, if this has been covered with a thin layer of glycerine and spirit.

FIG. 3.

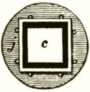

FIG. 4.

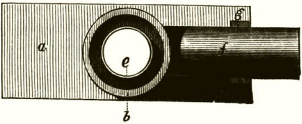

FIG. 3.—A view of the upper surface of the disc of thin brass *j*. The square of thin glass *c* is also shown in position.

FIG. 4.—A view of the upper surface of fig. 3 (the cap *d* and the disc *j* being removed). *a*, brass plate to which the cylinder *b* is soldered, and into which the smaller cylinder *e* is screwed; *f*, glass or brass tube cemented into the cylinder *b*, and to the step *g*, *g*.

When in position the disc *j* rests on the upper edge of the cylinder *b*, as shown in fig. 5. The thin glass *c* is kept in position by the short pins along its edge, these being screwed into the disc *j*. The india rubber tube *i*, *i*, and the mouth-piece *h*, are supposed to be removed.

These various modes of testing the atmosphere readily detected the presence of pollen, but were not to be depended upon in determining the quantity, and consequently the simpler and more reliable plan of exposing glass slides to the open air was adopted. The daily examination of the slides under the microscope showed that the rise and fall in the quantity of pollen in the atmosphere, and the intensity of the symptoms corresponded very closely.

Observations made in 1867 showed that pollen was sometimes carried over the city, and deposited on the glasses after being carried three to four miles. Further experiments of this kind were made by means of a kite to which were attached instruments that collected the pollen at high altitudes. One of these is shown at figs. 5 and 6.

FIG. 5.

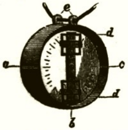

FIG. 6.

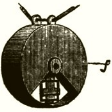

FIG. 5.—A view of the instrument with the cap *f* (shown in fig. 6) removed; *a*, a case of thin brass in which the wheelwork is placed; *b*, an arm of thin steel or brass, which is made to fasten on to the pivot shown at its centre. The pieces which project beyond the cross bars at each end are small steel springs, which are turned up at right angles at the ends, so as to keep the squares of thin glass in position. At each end the cross bars are turned over the glass in the form of hooks; *c*, the dial plate, marked so that each division represents a period of fifteen minutes when the central arm is moving; *d, d*, squares of thin microscopic glass bordered with black, so that a cell one centimètre square is formed upon them. These cells are charged with the prepared fluid, as in the other experiments; *e*, small rings attached to the case: through these the piece of cord passes which is attached to the cord used to raise the kite.

FIG. 6.—A view of the instrument with the cap *f* in the position it is when in use. This latter should be so constructed that it will not sink below the anterior margin of the case, *a*, as shown by the termination of the dotted line at *a*.

Drawn to a scale of ⅓rd.

This instrument was devised for the purpose of detecting the presence of pollen at high altitudes only, and is so constructed that it can be raised to any desired altitude before the glass on which the pollen may be deposited is exposed to the wind. The average of the observations made in different years showed that we have *more than nineteen times the quantity* of pollen in the upper atmosphere that we have in the lower. The highest altitude attained was two thousand feet, but on the method adopted there is no assignable limit to the height that may be reached, and what may be the result of more extensive experiments in this direction it is impossible to say. The upper atmosphere is at present almost an unknown region. One of my reviewers in speaking of these observations has said "they supplement the experiments of Dr. Angus Smith, and if repeated may give us that information about the upper air which Carpenter and Wyville Thompson have obtained, and are obtaining about the depths of the ocean." I hope some day to have time and opportunity to penetrate further into this almost unknown region.

So far pollen had been applied only to the mucous membrane of the nares, but it was found by subsequent experiments that wherever applied it produced disturbance. A decoction of pollen applied to the conjunctiva brought on congestion of the vessels, and this after a time was followed by severe chemosis. When fresh pollen was applied to an abraded portion of the skin œdema of the subcutaneous cellular tissue was produced, but there was no inflammation of the true skin. An important and interesting question is how pollen produces all this disturbance. When placed under the microscope and breathed upon as it is when in the nares, the pollen grain first begins to swell, then the granular matter alters its position and eventually escapes by bursting through the *intine* or inner membrane, and whilst this is going on it will frequently move half way across the field of the microscope.

At the time my researches were published I had not fully determined the special cause of some of the symptoms of hay-fever. After repeating many of the experiments to which I have briefly alluded, and after closely studying the subject anew I have come to the conclusion that the influence which pollen exercises upon the mucous membranes and other tissues is of a mixed kind. The sneezing is, I think, due partly to mechanical and partly to physiological action. The inflammation of the conjunctiva is probably due to mechanical action entirely. The chemosis of the conjunctiva as well as the œdema of the submucous and subcutaneous cellular tissues are, I believe, entirely owing to the physiological action of the granular matter. When, however, pollen is applied to the skin after this has been abraded there is this curious anomaly in its action, namely, that whilst œdema of the subcutaneous tissue is produced the *cutis vera* apparently escapes its action altogether. It is this œdema of the various tissues which constitutes the great peculiarity in the influence of pollen.

Another question that remained unsettled at the time my work was published was the determination of *the actual weight of pollen necessary to bring on an attack of hay-fever*. The solution of this problem I found to be more difficult than that of any with which I had had to deal. The whole matter hinged upon the average weight of single pollen grains. If this could be ascertained the rest would be comparatively easy. Again and again attempts had been made to weigh on the balance a number of pollen grains, such as could be counted under the microscope, but again and again I had failed. The largest number that could be counted accurately in a space of one square centimètre was three thousand, but this number did not affect a balance that turns easily with one *two hundredth of a grain* (one of Oertling's). I began to think I should have to give up the task without accomplishing anything more. I did not like to acknowledge this, however, and still persevered in my efforts and by the aid of the microscope, the balance, and the instrument shown in fig. 7 I have I think been enabled to solve the problem satisfactorily.

In using this instrument the screws K K K are first adjusted so that the points are about *one line* below the mouth of the graduated tube (equal to four turns of the screws). The screw I is now turned down until the compressor J has driven the air from the india-rubber tube. We now weigh on the balance $\frac{1}{100}$th of a grain of pollen and place it in one hundred grains of a fluid composed of *six* parts *of alcohol* (proof spirit) *two of glycerine* and *two of*

FIG. 7.

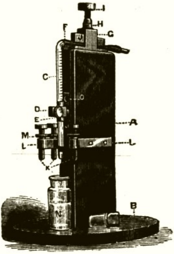

Fig. 7.—A, a broad flat pillar of wood, to which is attached the foot-piece B. C, a glass tube with an internal diameter of about $\frac{1}{16}$th of an inch, and graduated so that each division will contain $\frac{1}{20}$th of a grain of distilled water. D, a brass nut, into the posterior portion of which is inserted the small brass tube which carries the graduated tube C. The nut and the tube are slit perpendicularly, so as to permit the glass tube to be clamped by the screw E. F, a caoutchouc tube attached by one extremity to the graduated tube C, and closed at the other by a glass plug. G, a brass box open at each end for the passage of the compressor J. To the top of the box G is attached the nut H, through which passes the screw I which acts upon the compressor J. K K K, three screws which pass through nuts cut in the bars L L. Two nuts are seen in the posterior bar and one in the anterior one. These screws are used for regulating the distance of the microscopic slide from the mouth of the graduated tube C. On the upper part of the screws K K K are seen three lock-nuts M used to fasten the screws in any given position. N, the fluid containing the pollen. O, a flat plate of brass into which is rivetted the nut D. This plate is screwed to the edge of the pillar A. The lower part of the graduated tube is ground with fine emery powder, so as to cause a constant amount of capillary attraction. The ring of black varnish shown at the lower end of the tube prevents the fluid from rising beyond the lower margin of the ring. The screws K K K and I are cut with fifty threads to the inch, and the heads are graduated with twenty divisions on each, so that each degree gives a rise or fall of $\frac{1}{1000}$th of an inch.*

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* In the first form in which this instrument was used the graduated tube was placed on the top of the pillar, whilst a plain tube occupied the place of the graduated one. The compressor was in this case fastened to the posterior edge of the pillar A.

distilled water. After this has been well shaken so as to distribute the pollen evenly through the liquid, the bottle is placed under the tube C and raised until the point fairly dips into the liquid. The screw J is now turned up until the fluid rises to the uppermost mark of the graduated tube. If the screw is now turned gently down again until the upper surface of the fluid has passed *five divisions* a drop of the fluid equal to one fourth of a grain will hang from the mouth of the tube. This drop will contain 0·000,025 of a grain of the pollen. A microscopic slide with a circular cell of varnish upon it, half an inch in diameter, is now made to touch the points of the screws K K K and the fluid will at once be distributed over the surface of glass within the ring of varnish. The slide is now placed in the horizontal position and kept at a temperature of 100° or 120° Fahr. until the alcohol and water have evaporated and the glycerine is left as a thin and smooth layer. By placing the slide under the microscope with a good ¼ in. objective of moderate angle the pollen grains can easily be counted on any microscope that has a mechanical stage attached to it, if the method described at p. 126 of my work is followed.

On this plan the average weight of several species of pollen grains was ascertained. In each case ten slides were counted in order to neutralise possible errors. Ten slides of the pollen of *Lolium perenne* had an average of 150·8 on each slide; thus it was found that one grain, by weight, of this pollen would contain 6,032,000. Ten slides of the pollen of *Plantago lanceolata* contained 253·8 on each slide, so that it would require 10,124,000 to make up one grain by weight. Ten slides of the pollen of *Scirpus lacustris* gave an average of 620·5. Thus one grain by weight would contain 27,302,000 pollen grains. The pollen of the *Vacoa* (an exotic) contained 37,888,000 in one grain.*

It is necessary to remark here that the weight of the single pollen grain differs in different years. In a number of experiments tried in 1874, one grain of the *Lolium*

* I have also weighed the spores of two or three of the cryptogams. The spores of one of these weighed rather less than the 1—500,000,000 th of a grain. Of these, I may have something to say at another time.

perennè was found to contain 4,400,000. At § 234 of my work I remark that "in addition to those influences which make pollen more or less capable of fulfilling its own proper function in the vegetable world, there also seems to be some influence at work which, independent of the quantity of the *materies morbi*, or condition of the patient, alters its power of producing hay-fever." I believe now that this difference is mainly owing to the difference in the size of the pollen grain, and that this again is dependent upon the kind of season. In late and cold seasons we shall have ill developed pollen. In warm seasons we shall on the contrary have large and vigorous pollen, and just in the same proportion will the intensity of the symptoms vary in any given year. The calculations which follow are based on the results of experiments specially made this summer (1876).

We are now in a position to determine the weight of pollen necessary to bring on the malady. For this we have already some data collected. We know for example that the quantity of pollen deposited as compared with that inhaled in a period of twenty-four hours is as 1·0 to 4·4. But as a patient is not in the open air exposed to pollen more than eight hours out of the twenty-four, it will be necessary to reduce the 4·4 to 2·0, or less than one half.

The quantity of pollen collected on the day when the disorder was fairly commencing was 74, and if we multiply this by 2·0 we have 148 as the product. The pollen of *Lolium perennè* contains 6,032,000 in one grain by weight, and as this is a fair average of the size of the pollens of the English meadow grasses we may take it as a standard. If the number inhaled be divided by the number contained in one grain of this pollen we get the exact weight of pollen that will bring on the disorder. Thus $\frac{148}{6,032,000} =$ ·0,000,245 gr. or in other words less than $\frac{1}{40,000}$th of a grain inhaled in each twenty-four hours suffices to bring on the malady in its mildest form.

When the quantity of pollen in the atmosphere was the largest and the symptoms of the disorder were the most severe of any day in the season the deposit was 880 in the twenty-four hours; $880 \times 2 = 1760$; and $\frac{1760}{6,032,000} =$ 0·00029 grain. Thus rather less than $\frac{1}{3427}$th of a grain of pollen inhaled in each twenty-four hours will keep up hay-fever in its severest form.

The way in which pollen is distributed on the mucous membrane when inhaled may partly account for the effect which so small a quantity produces. And here it is important to notice two facts to which Mr. Darwin kindly drew my attention in 1873. 1st. Pollens have been divided into two classes, namely, into *coherent* and *non-coherent*. The pollen masses of the orchids may be taken as a type of the first class, whilst the pollen of the grasses may be taken as a type of the second class. 2nd. Delpino has also divided plants into two classes according to the mode in which they are fertilised. In the one case they are fertilised by the agency of the wind and are termed "*anemophilous*" plants. In the other they are fertilised through the agency of insects, and are termed "*entomophilous*." The grasses are examples of the first class and the orchids of the second.

Coherent pollen is seldom or never found floating in the atmosphere, and cannot therefore be a cause of hay-fever. The grains of incoherent pollen are always found floating in the atmosphere singly. In no case have I ever found a number massed together or one pollen grain over-riding another on the exposed slides. It must, therefore, be that the pollen grains will be distributed in the same manner on the mucous membranes. Each one will have its own separate sphere of action in which it can expend its full power without let or hindrance, and without waste of power. We cannot with any means we have at present at command show the exact nature of the action which pollen has upon the mucous membranes; nor do we know whether the œdema which it sets up in the submucous and subcutaneous cellular tissues is due to its action upon the capillary blood-vessels or upon those of the lymphatics. But upon whichever set of vessels its power is exercised we know that the granular matter of each individual pollen grain will have its own sphere of physiological action, and that the quantity of the *materies morbi* which operates within this sphere must be exceedingly small.

The interest shown in some of the questions I have brought under your notice has led me to give not only my new observations, but also to sketch briefly the course I have pursued in former experiments, and thus to some extent to go over old ground. This will, however, have made my object more clear to you, and will have grouped together most of the facts on which my latest conclusions are based. With one solitary exception in the matter of the genesis of hay-fever I have tried to avoid forming hypotheses. I have simply endeavoured to interrogate nature, and as faithfully as I could to record her answers. I might now legitimately draw what seem to me important conclusions from the facts I have given, but this I will not attempt to do because I feel sure that each individual mind will be able to do this for itself in a more forcible and suitable manner than I can hope to do, and I shall therefore leave each one to draw such lessons as the facts seem best calculated to teach.

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p 14 (Weight of pollen-grains)

p 876 — 405 [illegible] on pollen-gra

a Typha pollen 144 grain