bleeding, and then administer salines. In the other 14 cases so treated the condition of the patients permitted of the delay necessary for preparatory treatment and for the removal of all blood clots from the abdomen.

The crisis having passed, and when the case is first seen subsequent to the formation of a distinct and encapsulated hæmatocele, more conservative treatment is warranted. With rest in bed the majority of such cases undergo complete absorption, the only indication for operative interference being the possibility of secondary rupture of the hæmatocele demanding cœliotomy, or infection of the sac, which is best treated by vaginal incision and drainage. Against an entirely expectant line of treatment the element of time has to be considered, especially with hospital patients. Large hæmatoceles may take weeks to undergo complete absorption, which loss of time may be prevented by the safe proceeding of vaginal incision and drainage. Of my six cases so treated five were typical cases of retro-uterine hæmatoceles, and the patients left the hospital within three weeks from date of admission. In the remaining case of hæmatoma, abdominal section having shown that the blood was encapsulated in the broad ligament, the abdomen was closed and the case further treated by vaginal incision and drainage.

Dundee.

PROPHYLACTIC INOCULATION AGAINST HAY FEVER.

BY L. NOON, B.C. CANTAB., F.R.C.S. ENG.

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HAY fever is a form of recurrent catarrh affecting certain individuals during the months of May, June, and July. It is caused by a soluble toxin found in the pollen of grasses. The patients present the idiosyncrasy of being sensitive to this toxin, which is innocuous to normal individuals. The idiosyncrasy may be detected during any season of the year by dropping a little of an extract of grass pollen into the eye of the suspected individual; a reaction, described more fully below, will be obtained in the case of a hay fever patient, but a normal man will show no effect.

Bostock (1819)[1] recognised the seasonal recurrence of hay fever as separating it from other forms of catarrh. Blackley (1873)[2] advanced much evidence in favour of the pollen theory of its causation, but we owe chiefly to Dunbar (1903)[3] the exhaustive scientific proof of this theory. Dunbar showed that not only all the mucous membranes but even the skin of hay fever patients is sensitive to pollen toxin in a way not shown by normal individuals. He also proved that the injection of the pollen toxin gives rise in animals to the production of an antitoxin having a specific power of neutralising this toxin. Further, in hay fever patients, he showed the occurrence of some of the reactions associated with the production of immunity:—namely, a specific precipitation of pollen extracts by the patient's serum, and the phenomenon of complement deviation, during the hay fever season, and persisting for a short time after this. Pollen toxin is, therefore, a body capable of giving rise to the production of antibodies in animals and even in hay fever patients, subjected to its action. It is also undoubted that hay fever patients sometimes become cured of their idiosyncrasy. The most reasonable explanation of this phenomenon would seem to be, that the cured patients have had the good fortune to develop an active immunity against the toxin, to the action of which they have been liable for so long.

The repeated absorption of toxin at short intervals is, however, more likely to induce a condition of hypersensibility, and this is the more usual fate of the patient, who becomes only more sensitive during each succeeding season. The local application of a specific serum, such as pollantin, offers a reasonable method of treatment, but one which is difficult and laborious, and which is not calculated to bring about a permanent cure. Cures are, indeed, ascribed to the use of this remedy, but admittedly in exceptional cases; and where the conditions are not understood and the experience is not constantly repeated, one must hesitate to attribute the result to the cause cited. On general grounds a much more satisfactory result would be expected from the induction of an active immunity, and it seemed worth while to put this expectation to the test of experiment. The questions to be answered are as to what degree of immunity can be induced in hay fever patients by inoculations of pollen toxin, how these inoculations may best be regulated, and whether the affection can by this means be permanently cured.

With this end in view the experiments here described were undertaken in the past autumn, winter, and spring to study the reaction of hay fever patients towards inoculations of pollen toxin. The off season of the year, when the patients were not exposed to spontaneous inoculations, was favourable to this investigation, as the scheme of dosage was then not liable to be upset by spontaneous absorption of toxin from the air, laden with actively poisonous pollen grains. The plan of experiment was to obtain a numerical measure of the sensitiveness of the patients to the pollen toxin and to observe whether this was increased or decreased by subcutaneous inoculations of various quantities of pollen toxin. These observations can be conveniently carried out by the method described below, and it was found that, with well-regulated dosage, it was possible in every case to raise the patient's resistance, to a marked degree, within the lapse of a few months, while, on the other hand, ill-regulated dosage was at once made evident by a decrease in the resisting power.

The pollen extract used was prepared by Dunbar's method of extraction with distilled water, aided by freezing and thawing several times. The extracts were boiled for ten minutes after having been sealed in glass tubes; this treatment was not found to decrease their activity at all. The pollens tested were grass pollens of different species—*Phleum pratense*, *Poa trivialis*, *Holcus lanatus*, and *Agropyrum caninum*. These pollens were all found capable of exciting an energetic reaction when instilled into the conjunctival sac of hay fever patients. Timothy grass (*Phleum pratense*) was found to yield the most active extract, and this extract was consequently used throughout the rest of the experiments. One gramme of pollen was extracted with 50 c.c. of water. The activity of this extract may be judged from the fact that one drop of a five thousand-fold dilution is sufficient to excite a distinct reaction in the conjunctiva of the more sensitive patients.

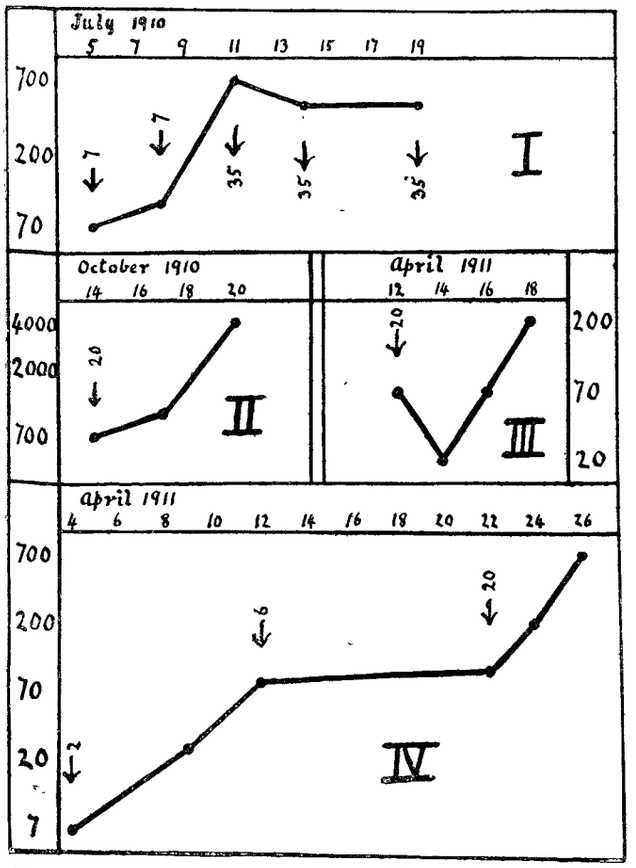
In order to express the strengths of pollen extracts used in testing patients and the doses of pollen toxin given subcutaneously, a unit of pollen toxin has been arbitrarily chosen. This unit is the quantity of pollen toxin which can be extracted from the thousandth part of a milligramme of Phleum pollen, and it has the advantage that all the quantities used can be expressed in whole numbers. The strength of a pollen extract is given below in terms of the number of such units contained in a cubic centimetre of the extract. Extracts of other pollens have been standardised against the Phleum extract by comparative tests on the eyes of hay fever patients.

A measure of the patient's resistance during the experiments is obtained by observing the strength of pollen extract necessary to excite a conjunctival reaction. One drop of the diluted extract is instilled into the eye. The reaction obtained consists in a reddening of the caruncula and, to a lesser degree, of the palpebral conjunctiva, together with a slight injection of the vessels of the ocular conjunctiva and some lacrymation. The patient experiences a feeling of burning and itching. These signs reach a maximum in about five minutes, and a little later there may be a slight attack of sneezing. The reaction lasts as a rule about half an hour. The strength of the extract, which is just sufficient to give this reaction, is used to describe the resistance of the patient. The most sensitive patients examined gave before treatment a distinct reaction with a dilution containing only 4 units per c.c., their resistance is described as 4; the least sensitive reacted to a strength of 70 units per c.c., or, in other words, had a resistance of 70. Normal individuals fail to react with the strongest extract (strength 20,000 units) and even resist the application of fresh pollen dust to the conjunctiva. Their resistance is therefore, by our scale, more than 20,000, but it is not infinite as a cubic centimetre of this extract injected beneath the skin of a normal man has been

[1] John Bostock: Medical and Chirurgical Transactions, vol. x., 1819, p. 161.
[2] C. H. Blackley: Experimental Researches on the Causes and Nature of Catarrhus Aestivus, London, 1873.
[3] W. P. Dunbar: Zur Ursache und specifischen Heilung des Heufiebers, München, 1903.

found to give rise to a slight local swelling and tenderness, lasting for about 24 hours.

Course of immunisation.—Patients received subcutaneous injections of pollen extract. At first very minute doses were given at intervals of three or four days (Fig. 1), and the resistance of the patients rose rapidly; on increasing the dose, however, it was found that the resistance ceased to rise and even went back towards its original value. Longer intervals were then allowed to elapse between successive



The numbers at the sides denote the resistance of the patient, given in terms of the strength of pollen extract, one drop of which was sufficient te excite a conjunctival reaction. The arrows indicate subcutaneous inoculations of pollen extract, quantities given in the units described in the text. Figs. 1 and 2 refer to one patient at different periods of treatment; Fig. 3 shows the response obtained after about a month's treatment in another case; and Fig. 4 the early stages of treatment.

inoculations. The patient to whom Fig. 1 refers had a three months' respite and, after that interval, responded to a moderate dose in the way shown in Fig. 2. It is not necessary, however, to leave such a long interval as this between the doses: ten days or a fortnight are, as a rule, sufficient, and at the beginning of treatment, when small doses are being given, a week is enough (Fig. 4). After some time, when the resistance has been considerably raised, small doses cease to have any effect. On increasing the dose it is found that the first effect of the inoculation is to lower the resistance for a few days, giving a *negative phase*, after which the resistance rises again and passes beyond its former maximum (Fig. 3). Ultimately a stage is reached at which the resistance, as measured by the ocular test, ceases to rise, or rises so slowly that the alteration is only obvious after prolonged observation. At this stage the patients will withstand gradually increasing subcutaneous inoculations without showing a negative phase. In the early stages of immunisation it is possible, by an overdose, to induce a severe attack of hay fever lasting nearly 24 hours; this has not been observed in the later stages.

The result of these experiments so far is to show that the sensibility of hay fever patients may be decreased, by properly directed dosage, at least a hundredfold, while excessive or too frequent inoculations only serve to increase the sensibility. It still remains to be seen whether the immunity thus attained is sufficient to carry the patients through a season without suffering from their annual attacks of hay fever. Patients are under observation who have undergone treatment for periods varying from a few weeks to eight months.

It is hoped that these cases will afford material for a further report after the present hay fever season. This work is now in the hands of my colleague, Dr. J. Freeman, who very kindly came to my assistance and carried on the observations during my enforced absence of some months.

Devonshire-place, W.

A CASE OF

SUPPURATIVE ARTHRITIS OF KNEE-JOINT, DUE TO INFLUENZA BACILLUS, OCCURRING IN A BABY AGED SIX MONTHS.

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IN the present indefinite state of our knowledge regarding the bacillus of Pfeiffer and allied species, each case where such organisms are found demands careful study. The following is the first recorded case of an uncomplicated mono-articular suppurative arthritis due to the bacillus influenzæ, and it presents several features worthy of note.

A healthy baby, aged 6 months, began on Nov. 13th, 1910, to suffer from pain and swelling of the left knee-joint. She was first seen by a medical man on Nov. 19th, and, as she was feverish and the joint seemed much swollen, was at once removed to the Glasgow Royal Infirmary. The temperature on admission was 101·6° F. and the pulse-rate 128. On the 20th the temperature was 102·2° and the pulse-rate 170. On the 21st the joint was incised and a considerable quantity of pus mixed with blood was evacuated; a drainage tube was left in. After operation the temperature fell to normal; it afterwards went up to 100°. On the 27th the temperature was 99·2° and on the 29th it was normal. The child made an uninterrupted recovery, at no time presenting any symptoms which were not attributable to the condition in the knee-joint.

The previous history of the case was carefully inquired into, and it was found that the child had never before suffered from any illness, that she had shown no trace of whooping-cough or influenza, and that neither in her family nor in the immediate neighbourhood was there any case of these maladies.

Bacteriology.—Stained smears from the pus showed chiefly polymorphonuclear leucocytes and a tiny bacillus resembling accurately the bacillus Pfeiffer. There was a considerable amount of phagocytosis. Cultures were made on various media. Those on ordinary agar and bouillon yielded no growth, but those on blood agar showed a growth resembling exactly that of bacillus Pfeiffer—minute transparent "dew-drop" colonies, which always remained discrete, and which had attained their maximum development in 24 hours. Microscopically the appearance conformed entirely to that of bacillus Pfeiffer—one found a tiny, slender, pleomorphic bacillus, tapered at one or both ends, showing many "diplococcal" forms and occasional so-called "filamentous" forms which measured five or six times the normal length. The organism was non-motile and Gram-negative; it stained feebly with the usual basic dyes, such as methylene or toluidin blue. Besides growing on blood agar and blood bouillon the organism grew well on a "staphylococcus agar" made by melting a tube of ordinary agar and adding to it ½ to 1 c.c. of a sterilised emulsion of staphylococci in saline solution.[1] It is immaterial whether

[1] This medium had been found by my colleague, Dr. A. Campbell, to be an excellent medium for bacillus Ducrey. In connexion with the growth of bacillus Pfeiffer, Grassberger had noted that on tubes where there were colonies of staphylococcus aureus any colonies of the former germ which might be in the neighbourhood took on an exceptional development. Rosenthal had found that a dead culture of staphylococcus had a similar "favourising" effect. If one sterilises an agar culture of staphylococci in the autoclave and then pours it into a Petri plate and adds some blood to the medium one finds that it forms an exceptionally favourable culture-ground for the bacillus Pfeiffer. Rosenthal considered that this "favourising" action was due to substances secreted by the staphylococci into the medium or to a modification of the medium under the influence of these microbes. Allen found that a bacillus influenzæ which refused to grow on ordinary blood agar could be got to grow when 2 c.c. of sterile bouillon culture of staphylococcus were added to it. The above-mentioned medium which we used required no addition of blood and did not require the presence of the medium on which the staphylococcus had grown. The "favourising" action is here obviously due to the staphylococci themselves or to such products as are washed off from the surface of an agar slope by the salt solution.