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PAROXYSMAL RHINORRHŒA.*

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MY object this afternoon is to give a general or rather a pathological survey of paroxysmal rhinorrhœa; but neither to deal with its history, nor, since I am not a laryngologist, to give the laryngological view of it.

However, I thought it best to begin by finding out what the laryngologists themselves have said about paroxysmal rhinorrhœa, and on looking up the records of discussions I was delighted to find that not only was hay fever taken as the typical example of this condition, but that the speakers seemed to spend two-thirds of their time discussing it.

Let us start then with a rough definition of paroxysmal rhinorrhœa as *a symptom-complex in which the pathological mechanism runs parallel with that of hay fever.*

I propose to give you the pathological mechanism; therefore let us examine at once the essentials of our type—hay fever.

(1) The first point to be emphasised is that whereas the pollen of the grasses is quite innocuous to the normal person, it invariably causes distress whenever it comes into contact with the living tissues of hay-fever subjects. This is perhaps the most striking of all immunological phenomena. I have frequently given myself, with impunity, at least twenty times what to some hay-fever subjects would be a fatal dose of pollen. To a rabbit I have given 20,000 times the human

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"lethal dose." In fact, the material is completely non-toxic to the normal animal. But in the hay-fever subject, whenever grass pollen reaches the mucous membrane in the form of atmospheric dust, then paroxysmal rhinorrhœa is produced; so that we can now develop an original definition and say that paroxysmal rhinorrhœa is *the symptom-complex produced whenever a foreign protein comes into contact with the nasal mucous membrane of a person who is sensitive to that protein.*

(2) These foreign proteins are legion. They include any animal or vegetable substance in the atmospheric dust; dermal scales from animals, all the pollens of plants, all the spores of all the fungi and other lowly organised vegetables; also vegetable substances such as wheaten flour, sawdust, etc. Many of these are almost as easily detected as the grass pollen; others, such as the spores of fungi, are rarely, if ever, identified as the causal agent.

(3) Now the inspired air is not the only route by which foreign proteins reach the nasal mucous membrane and so produce paroxysmal rhinorrhœa. The irritant may arrive through the blood, *e.g.* from a bacterial toxin, or from some food substance absorbed from the alimentary canal.

That the foreign proteins can arrive both by the air and by the blood has been a commonly accepted fact for years, but to give a laboratory demonstration on this point I have in the case of two perfectly normal men, constructed two artificial paroxysmal rhinorrhœas, one in which the protein was carried through the inspired air, the other by way of the blood.

(*a*) In the first I sensitised (with the aid of Mr Waggett) the mucous membrane of my colleague, Dr Hare, with the serum of a hay-fever subject; the result was that when he sniffed up a little grass pollen to-day he at once began to sneeze, and if he is in the room at this moment you will find his pockets stuffed with some half dozen thoroughly saturated pocket handkerchiefs. Thus an artificial rhinorrhœa was successfully produced by an irritating air-borne pollen.

(*b*) In my second experiment the middle turbinal of my own nose was sensitised with the serum of a person who becomes ill whenever she eats eggs, with the result that after drinking an egg-flip this afternoon, my nose has been itching and uncomfortable. I rather spoiled the experiment by having too much cocain in the nose, the effect of which had not

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completely passed off before I drank the egg-flip. In this instance the irritant passed from the mucous membrane of the stomach to the mucous membrane of the nose by the blood-route.

It is clear, therefore, that paroxysmal rhinorrhœa will occur whenever a foreign protein irritant reaches the mucous membrane of the nose of a person who is sensitive to that particular protein, whether it be carried by way of the blood stream or by way of the inspired air.

In laryngological practice hay fever is more or less a laryngological disease, but pathologically it most certainly is nothing of the sort.

(1) Even in the naturally occurring disease the eye of the sufferer, according to my statistics, gives more trouble than the nose; a few patients complain more of the skin of the face than of nose or eye symptoms together, and others are troubled by the general upset and complain of neurasthenia and so on, rather than of any local nasal symptoms.

(2) Further, when one brings grass pollen artificially into contact with the tissues of a hay-fever subject in a site other than the mucous membrane of the nose, it becomes clear that the rhinorrhœa of hay fever is merely a botanical accident. For example, if pollen is placed in any part of the cutis vera of a hay-fever patient, a very marked urticarial wheal, surrounded by a crimson flush, will develop in from fifteen to twenty minutes, and the patient will suffer irritation at the site of contact. Dunbar placed pollen in the rectum of a hay-fever subject and produced pruritus ani. I have put pollen into the food of another subject, and produced nausea, giddiness, vomiting, and diarrhœa, though it is easy to show that the normal person can eat quantities of pollen without any ill effect whatever.

Again, if the pollen is injected into the vein of a hay-fever subject, and is given, so to speak, the entire body to choose from in the matter of symptom production, giant urticaria, migraine-headache, angio-neurotic œdema, perhaps asthma, will appear, and possibly some rhinorrhœa: but it is quite obvious that the last is neither the earliest nor the most striking symptom to be produced.

(3) A still more convincing experiment can be performed to show that the trouble is a constitutional one, that it exists in fact in the very blood of the patient. If a small amount

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of serum from a hay-fever case is injected into the skin of a normal man, the area of skin injected will become grass-pollen sensitive, and will remain sensitive for one or two weeks. This may be demonstrated by bringing pollen into contact with the small sensitised area, or else by injecting pollen into the blood stream of the experimental person, when it will produce no symptoms whatever on the rest of the body, but at the site of the injection a swelling comparable with angio-neurotic œdema will be produced.

(4) Parallel experiments can be formed with any of the other proteins capable of producing paroxysmal rhinorrhœa, so that I think I have shown you in detail why I claim that it is not a laryngological disease, but merely a local manifestation of a general sensitiveness.

I will now give you a list of other manifestations of protein idiopathy. The list is admittedly incomplete, but will be of use in *two* directions.

Paroxysmal rhinitis ("nasal asthma")
HF. Hay fever.
H. Horse asthma (cat asthma, etc.).
A. Asthma.
U. Urticaria.
Eczema.
Angio-neurotic œdema.

F. Food sickness (vomiting, diarrhœa).
E. Epilepsy.
M. Migraine.
Paroxysmal arthritis.
Paroxysmal colitis.
Paroxysmal nephritis.
I. Insect fever.

(1) The presence of any of these other protein idiopathies will make the occurrence of paroxysmal rhinorrhœa the more likely, for they are sister-symptoms.

(2) Further, any generalisations that may be arrived at regarding, let us say, angio-neurotic œdema or asthma, will be applicable to our subject.

I have no time to-day to offer definite proof that these other protein idiopathies *are* sister-symptoms, but the fact is nowadays fairly generally recognised.* Before leaving the list, however, I should like to say that while some of the items (*e.g.* paroxysmal colitis and nephritis) are new-comers, there is no reason to believe that the list is complete.

To turn to the pathological mechanism of these protein idiopathies, and of paroxysmal rhinorrhœa in particular, it would be bad philosophy to speak of the protein irritant as

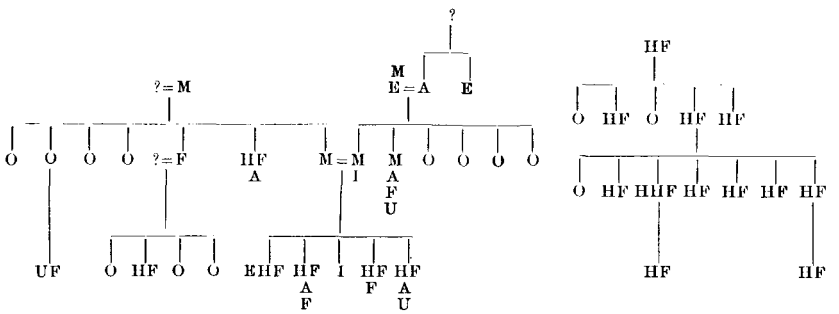
* *Proc. Roy. Soc. Med.*, 1920, xiii., 129-148.

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the cause. One must rather think of a causal chain in which the protein irritant is merely one of the links.

I give here a very incomplete list of such causal links: (i) Diathesis (heredity); (ii) protein irritant; (iii) nervous factors; (iv) trauma (regional factor).

(i) Of the first of these four, namely, diathesis, we know little or nothing. The marked hereditary incidence is very noticeable, but hay fever has been known to show itself in a patient for the first time at the age of 74; he had numerous hay-fever blood relations and he had been absolutely immune up to that point. I append two hereditary charts chosen at random, one of them to illustrate the enormous incidence of hay fever in one family; the other to illustrate how a family may inherit not one particular protein idiopathy only, but an apparently indiscriminate mixture of them.



The above two charts show the hereditary incidence of the protein idiopathies. The first one shows six cases of hay fever and a large mixture of other protein idiopathies; the second is almost entirely concerned with hay fever. The explanation of the various letters and symbols is given in the left hand margin of the list of protein idiopathies given above. The symbol "O" is put in to signify that the person was, as far as could be ascertained, normal in relation to foreign proteins, *i.e.*, possessed no protein idiopathies.

(ii) The protein factor I have said enough about already; it is the complement of the diathesis factor.

(iii) The third, or nervous, factor becomes very obvious when one collates observations on a large number of these protein idiopathies, paroxysmal rhinorrhœa included. The only conclusion concerning hay fever given in the edition of Osler's *Medicine*, which I consulted, is the statement that a woman got an attack of hay fever by smelling an artificial rose, and that, therefore, "the whole disease is a neurosis." When I started working at hay fever fifteen or sixteen years

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ago, nearly every patient that came to me had been told by his or her doctor that it was "all nerves"; and, indeed, any one of us can demonstrate that nerves have something to do with it by producing an attack of hay fever in the sensitive subject (though this can be done in the pollen season only), by mere suggestion or word-painting of the particular object or incident to which he attributes his symptoms. Over and over again one hears of hay fever, or any of the other protein idiopathies, being produced by some emotional disturbance—bad news, excitement, danger, eroticism, emotional music, and so on; and apparently the attacks may be terminated in the same way. Yet, while it is perfectly true that the more "jumpy" and "nervy" the subjects are, the more likely they are to have attacks of some protein idiopathy, anyone who has examined large numbers of these cases will, I think, agree that taking them all in all they are not more mentally unstable than, let us say, any chance collection of medical men. And if that is disputed I can say this: I have shown that paroxysmal rhinorrhœa can be artificially produced in a perfectly normal man by the transference of serum from a hay-fever patient. Supposing that hay fever is "all nerves," is it then suggested that the nervous mechanism of the patient must be transferred with the serum to the normal man, before the reaction at the sensitised area can be brought about? I think not. Even here nerves do come into play, but they are the nerves of a normal man.

(iv) Trauma is my fourth link in the chain; there must be something to account for symptoms arising in one particular place. In hay fever the atmospheric method of arrival is no doubt the chief localising cause; but in angio-neurotic œdema, for example, it is very noticeable that slight injuries to the skin may determine the exact site of the swelling; and, again, in epilepsy, injury to the head may predispose the sufferer to an epileptic fit in exchange for, let us say, eczema or asthma, or paroxysmal rhinorrhœa.

Such are the bare outlines of the pathology of paroxysmal rhinorrhœa. With diagnosis and treatment I have no time to deal, but I should like to make just one point about each. People used to say, and some still say lightheartedly, "identify the foreign protein and deal with that." But this is not so easy. There are not hundreds but thousands of these proteins, and a patient may be subject to many of them, so that you may

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identify dozens by experiment without coming across the one which is causing havoc. Again, in the artificial skin-reaction method, many of the largest protein groups (for instance, bacteria, spores from the moulds) give next to no reaction compared to food proteins, or still more the pollens and the dermal scales from animals. When, however, the protein cause can be identified, this is of course well worth doing.

As for treatment, I will only say here that every specialist will deal with the link in the causal chain which concerns his own province; I, as immunologist, would wish to deal with the foreign proteins by avoidance or desensitisation, and that still seems to me by far the most helpful line of treatment. The psychologist or neurologist would of course want to work on the nerve factor, not, I think, so helpfully. The laryngologist in dealing with paroxysmal rhinorrhœa would quite properly wish to treat whatever abnormal local conditions he might find.

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