

AN INVESTIGATION
INTO THE LITERATURE REGARDING
NASAL ALLERGY
WITH SPECIAL REFERENCE TO
THE THERAPEUTIC VALUE OF
ZINC IONISATION -
A REPORT ON 120 PERSONAL CASES.

Presented as a Thesis for the Degree of
Doctor of Medicine

by

John Frederick Birrell,

M.B., Ch.B.(Edin.), F.R.C.S.E.



INTRODUCTION.

There can be few lines of treatment for any condition within the realm of Ear, Nose and Throat work that have provoked so much controversy within recent years as has zinc ionisation for nasal allergy. Many workers are enthusiastically in favour of it, while just as many are strongly opposed to it. It is with a view to collecting the opinions of others and contrasting them with my own experiences that I present this paper. What, if any, is the true value of zinc ionisation? Which cases derive most benefit from it, and which are not helped at all? What are its advantages and dangers? What, in short, is its place in modern therapeutics?

My own introduction to it came about in a curious way. A young woman presented herself at the Ear, Nose and Throat Department of the Royal Infirmary of Edinburgh complaining of hay fever. She had read in a Sunday newspaper of a "wonderful cure" that was being used in London, and demanded to know whether we could supply the same treatment in Edinburgh. Thus it was that I first used the St. George's Hospital technique of zinc ionisation in Edinburgh. Later, I modified it slightly in order to enable more patients to have immediate treatment. Since that time - September, 1936 - I have treated 120 allergic patients in Hospital and /

and in private, and, in addition, a number of experimental non-allergic cases with a view to ascertaining whether ionisation had any effect on these. The results of the 120 cases I propose to analyse fully.

In order to collect a sufficient number of cases for a general survey of aetiological problems, I have looked through the records of a further 120 cases occurring in the Ear, Nose and Throat Department of the Royal Infirmary of Edinburgh. These will be used in a general way, and their treatment will not be analysed in any sense as some of them have had ionisation treatment from other members of the staff.

I have not attempted to make a series of pathological studies in the cases for, according to Hollender and Fabricant⁹⁶, biopsy is too restricted to yield sufficient or adequate information and, they say, the evaluation of the status of ionisation must be made on clinical grounds alone. I have taken a number of specimens for personal interest, but no exhaustive pathological study has been made. Nor have I attempted to check the findings of the authors who have experimented with various solutions instead of zinc sulphate for ionisation purposes. The results given in this paper are purely clinical.

It is with pleasure that I record here my indebtedness to Dr. I. Simson Hall for the opportunity afforded /

afforded to me of treating an unselected series of cases appearing at his out-patient clinic over a period of two years. He has offered me many suggestions and has permitted me to make statistical notes on his allergic cases during 1939. I should like to thank also Dr. G. Ewart Martin for allowing me to make a statistical study of his nasal cases during the past year. Lastly, my thanks are due to Professor D. M. Dunlop for allowing me to treat a number of his asthmatic cases and to publish my results.

NOMENCLATURE.

There is a bewildering confusion of names applied to the various manifestations of the condition under discussion. To the whole group of diseases the term "allergy" was given by von Pirquet in 1906. He then defined it as an "altered reactivity of cells and tissues". "Atopy" or "strange disease" was applied to the condition by Coca and Cooke³³ in 1923.

Putting asthma to one side, as this is quite a definite clinical entity, we are left with cases of sneezing and watery rhinorrhoea of allergic origin. These may be seasonal or non-seasonal. The term "hay fever" holds pride of place to describe the seasonal variety. It is a name bestowed on the condition by the public and, as it has survived a century of usage, it is unlikely to be replaced now. It /

It is, however, an unfortunate term as the symptoms are not due to hay and there is no pyrexia.

The names applied to the non-seasonal or perennial variety are many. The commonest are - vasomotor rhinitis, allergic rhinitis, hyper-aesthetic rhinitis, paroxysmal rhinorrhoea, nasal hydrorrhoea, and atopic coryza (Forman⁶², 1934).

In this paper the terms asthma, hay fever and vasomotor rhinitis will be adhered to as far as possible.

HISTORY.

The earliest reference to the clinical manifestations of nasal allergy that I have been able to find in the literature is contained in Hansel's book on "Allergy of the Nose and Paranasal Sinuses"⁸⁹. There, in the historical part, he mentions that, in 1565, Botallus found that the perfume of roses produced sneezing and headache in some people. Van Helmont, who lived from 1577 to 1644, was the first to describe cases of familial summer itch. Bostock, of Liverpool, wrote in 1819 of his personal experience of a summer complaint associated with sneezing, and in 1828 he had collected and reported on 28 cases of "catarrhus aestivus" or summer catarrh. This was a recurring complaint starting between May and June and lasting from four to eight weeks. He made first mention of the name of hay fever which had been given to it by the /

the public. Heberder, of Guy's Hospital, called it "periodic spring catarrh". The association between the nose and asthma was described by Herek in 1844, while in 1872 Voltolini claimed to have cured eleven asthmatics by removal of nasal polypi.

Experimental work in connection with the inter-association of asthma and nasal mucous membrane was carried out by Sandeman in 1890 and Brodie and Dixon in 1903. They found that stimulation of the nasal mucosa in the "asthmagenic" area of the nose produced a bronchospasm akin to asthma. This asthmagenic area was shown to consist of the parts of the nasal cavities bounded by the sphenoidal and ethmoidal bones - i.e. the upper two-thirds of the nasal septum and the superior and middle turbinates and meati.

Francis⁶⁵, in 1902, surprised the British rhinologists by claiming nearly 50% of complete cures in asthma by the simple method of cauterising certain parts of the nasal mucous membrane. He concluded (i) that asthma is due to a reflex spasm of the bronchioles (ii) that the irritation might arise in the nose because of the onset of asthma noted after nasal injuries (iii) that asthma is not due directly to nasal obstruction and (iv) that some part of the nasal apparatus has a controlling influence on the respiratory centre.

THEORIES.

About 1920 the theories which underlie our modern conception of nasal allergy came under serious consideration. Sluder^{15'}, in 1919, believed asthma to be a reflex act from stimulation of the sphenopalatine ganglion, while Beck¹² in the same year put forward the theory that asthma was due to some derangement of the glands of internal secretion. In 1921 Caulfield²⁹ said that hay fever and asthma were manifestations of anaphylaxis, while Shea was of the opinion that vasomotor rhinitis resulted from protein sensitisation. Kaiden¹⁰⁸, however, in 1924 concluded that too much emphasis had been laid on protein sensitisation and too little on nasal and bronchial physiology. He was of the opinion that, with an unobstructed nose, irritants stimulated the bronchioles resulting in reflex nasal engorgement and the production of hay fever. If, on the other hand, the nasal airway were blocked by deviated septum or enlarged turbinates, the bronchioles became reflexly engorged with the production of asthma.

Kolmer¹¹⁴, in 1930, went a step further when he discussed two theories. The first was the widely accepted "cellular" theory which postulated that, when the exciting agent or allergen came into contact with the antibody in the sensitised cells of the nose, there occurred a colloidal shock reaction resulting in the production of lesions and symptoms.

The /

The other or "humoral" theory was that the exciting agents were present in the blood where they met antibodies with the production of an allergic reaction. Kolmer stated that the essential difference between normal and allergic persons is that the latter produce an antibody to pollens while the former produce no such antibody.

James Adam², who has done so much to forward the dietetic factor in aetiology, said in 1925, during a discussion on paroxysmal rhinorrhoea in the Section of Laryngology in the Royal Society of Medicine, - "the cause (of paroxysmal rhinorrhoea) is a toxæmia resulting from a carbohydrate excess especially in respect of milk foods interfering with the proper metabolism of the more complex protein molecule. The eosinophilia is the chemostatic response of the polymorphs to the acidosis so produced". He certainly supports his theory by quoting convincing figures in the cures of asthma by the abolition of milk from the diet. Adam also draws attention to the existence of "week-end" paroxysmal rhinorrhoea resulting from over-eating on Saturdays and Sundays.

Freeman⁷⁷, during the same discussion, stated that paroxysmal rhinorrhoea is a symptom complex produced whenever a foreign protein comes into contact with nasal mucosa of a person who is sensitive to that protein. These foreign proteins are legion - dust, dermal scales of animals, pollens, spores /

spores of fungi, wheaten flour, sawdust, etc. Blood-borne proteins may affect nasal mucosa as well as inspired protein. He demonstrated that it was possible to sensitise a normally insensitive mucosa and produce rhinorrhoea by inhalation and ingestion.

Stein¹⁵⁵, in 1923, in a survey of the hay fever question, said that the condition is due to a sensitisation the antecedents of which may be an "altered state of the fluids of the body". He wondered whether this was a chemical change, an alteration of balance or an endocrine disturbance. Fraenkel⁶⁴ amplified this in 1937 by stating that allergy is due to a para-sympathetic irritation produced by either metabolic factors, as shown by an altered potassium/calcium balance, or endocrine factors. The para-sympathetic system may be irritated by paralysing the sympathetic system, e.g. by adrenalin and pituitrin, or by stimulating the para-sympathetic system directly or indirectly, e.g. by atropin. Fraenkel goes on to say that "allergy usually begins with a hypersensitivity towards one or two well-defined allergens (monovalency). Gradually, however, if the condition does not receive proper treatment, the body becomes more and more sensitive towards other allergens (polyvalency)". He affirms that the only real proof of allergy to a specific allergen is the production of allergy by exposing /

exposing the person to the protein while its removal results in cure.

The association between sinus infection and nasal allergy - especially asthma - has been stressed by very many observers and the grossly divergent views expressed will be discussed more fully when the questions of X-ray examination and treatment come under consideration. Suffice it to say at this juncture that, on the one hand, Abbott¹ stated in 1914 that "ethmoiditis is a most constant and probably a necessary condition in the aetiology of asthma"; Gottlieb⁸² (1925) said that paranasal sinus disease may well cause asthma; and Haseltine⁹², in 1925, held the view that "the asthmatic patient has an abnormal ethmoid; anything that lessens ethmoid pathology will relieve him". Baum⁹ (1932), on the other hand was of the opinion that the histological findings "give rise to the erroneous belief that asthma is associated with sinus disease and to the futile attempts to cure it by extirpating diseased sinus mucosa".

Mention must also be made here of the work of Duke^{44, 45, 47, 49, 50, 51} and of Hansel^{86, 87, 88} who have been reviewing the advances made in the study of allergy and have published their results every year or two in the "Archives of Otolaryngology" and the "Journal of Allergy" respectively.

The position at present appears to be, then, that /

that the nasal mucous membrane, being richly endowed with autonomic nerve fibres, is liable to be affected by foreign proteins or other substances which can reach it either directly from inhalation or indirectly through the blood stream from ingestion. The result of such a stimulation may be seasonal or non-seasonal allergic rhinitis, or, reflexly, asthma.

It might be appropriate here to mention the pathway of the nasopulmonary reflex. Afferent fibres run from the upper part of the nasal cavities - the so-called "asthmagenic" area - to the Gasserian ganglion. This they reach by two routes - (i) via the anterior ethmoidal, naso-ciliary and ophthalmic nerves (ii) via the sphenopalatine nerves and ganglion. From the Gasserian ganglion impulses pass to the nucleus of the Vth nerve situated in the pons. This communicates with the nucleus ambiguus in the medulla and from there the vagus takes the efferent fibres to the bronchioles.

FACTORS.

It seems to be generally agreed that heredity, protein irritation, bacterial irritation, nervous elements and physical factors are all concerned to greater or less degree in the production of allergy in an individual.

Most observers agree that heredity is a definite and almost inevitable factor in the production /

production of allergy. It appears to be transmitted by the mother of the offspring as a dominant Mendelian characteristic. The frequency with which this occurs is described as varying from a very small percentage to about 75%. Whether all the offspring who inherit allergic tendencies necessarily become allergic is not so clearly understood. Piness and Miller¹³⁴ stated in 1929 that every individual with an allergic background is potentially liable to allergic disease. This does not appear, they say, if the tolerance is high; but if his "balanced state" (Vaughan¹⁶⁵, 1927) is lowered as by infection, change of environment or occupation, allergy will occur.

The question of protein sensitisation has been very fully worked out by Forman⁶² who published his conclusions in 1934. He divides allergy into four classes - (i) the hereditary allergics or atopic individuals (ii) those affected by bacterial allergy (iii) the contact allergics and (iv) those whose allergy is due to physical conditions.

Forman's first group is susceptible to allergens reaching the nasal mucosa either directly, or indirectly by means of blood or lymph channels. The inhalation proteins are met with seasonally or all the year round. Where the offending protein is a seasonal one, the result is hay fever, but where the nose is irritated throughout the year by some /

some protein a vasomotor rhinitis will result.

To make a complete list of these inhalation proteins is well-nigh impossible, but they can be broadly classified into:-

- (i) Seasonal proteins - pollens of various flowers and grasses, moulds (Bernton and Thom,¹⁵ 1933), spores of fungi.
- (ii) Non-seasonal proteins - emanations of various animals and fowl, human dandruff, house dust, (Cooke³⁶, 1922), soap powder, flour and other powdered proteins such as orris root and rice powder which are used in cosmetics. There are also those connected with trades such as factory dust, the fine wool dusts, chemicals, etc.

Similarly, no attempt will be made to make an exhaustive list of the ingestion proteins. They include nearly all the foodstuffs that are commonly eaten - eggs, milk, chocolate, wheat, peas, beans, potatoes, tomatoes, etc., etc. These proteins enter the blood stream from the intestine and are thus conducted to the nasal mucous membrane. Other proteins arriving at the nose in this way are injected proteins of extracts.

The complete group has been called by Forman the "specific sensitising substances". It is obvious that the mucosa must be prepared for the reception of these substances before allergy will arise, otherwise everyone would exhibit allergic manifestations /

manifestations. It is equally clear that such a preparation is most likely to be a hereditary predisposition.

Forman also makes a group of ^{what} ~~which~~ he calls "non-specific sensitising substances". In this can be included barometric changes, light, emotional upsets, worry, fatigue, focal infections, acute and chronic infections, constipation, and such bodily deficiencies as malnutrition, calcium loss, hypo- or achlorhydria and deficient ductless glands. He concludes by saying that if any sensitised person meets with one or more of the sensitising agents either a state of tolerance (Vaughan's allergic equilibrium), or a state of allergic reaction will be set up. The allergic reaction may be general or local and if the latter may affect the nasal or bronchial mucosa.

The question of bacterial sensitisation is interesting and vastly different conclusions are reached. The theory is that the surrounding nasal mucous membrane becomes allergic to the bacteria of a neighbouring infected sinus or - as Forman suggests - a focus of sepsis further away, whose bacterial proteins reach the nasal mucosa by the blood or lymph channels.

Ramirez¹⁴¹, in 1938, goes further with the question of asthma which he defines as a "bronchial neuro-cellular syndrome characterised by recurrent attacks of /

of paroxysmal dyspnoea". He divides asthmatics into allergic and non-allergic. The former group, which he calls bronchoedema, owe their attacks to inhalants, ingestants, injectants or focal infection; while the latter group, called bronchospasm, derive the stimulus from para-sympathetico-mimetics, reflex vagus excitants, local irritants or psychogenic and endocrine dysfunctions.

We see, then, that allergy may arise in persons who are sensitised by heredity and who obtain their allergy in the course of their ordinary daily life. They meet the allergens in their surroundings or their ordinary foodstuffs. Another group of people acquire allergy as a result of some change in environment or occupation or climate. One case which I encountered in this class was a woman who had no allergic family history and no personal allergic history until she married an ostler. She then gradually developed sensitivity to animal dandruff and suffered from paroxysmal rhinorrhoea each evening when her husband returned from work. She had a positive skin reaction to animal dandruff. Another girl had asthma which was due to her work. She worked amongst morphine and its derivatives in a chemical factory and was sensitive to them only.

Climatic changes are interesting though not easy to explain satisfactorily. Just^{'05}(1934), quoting the "miasma" theory of van Leeuwen, suggests that /

that they are due to the presence in the air of "colloidal substances of unknown composition". Reaction to strong sunlight is uncommon yet I have had personal experience since childhood of sneezing and epiphora on looking into a strong sun although I have not, to my knowledge, any other allergic manifestations.

Nor can the personal element be forgotten. Hamblin-Thomas⁸⁴ (1937) believes that the psychological factor is most important. Freeman⁷⁷ (1925) has said that the nervous element is not an invariable finding in allergy, but that the majority of the patients are of the "jumpy" type. Just¹⁰⁵, on the other hand, inclines to the view that the nervous element is negligible. In my own series of cases I found that those highly-strung people who were apprehensive of treatment responded more favourably than the plethoric manual labourers.

INVESTIGATION.

That allergic manifestations in the nose may be a common finding is shown by the fact that of 700 nasal cases Baum¹⁰ (1934) found that 191, or 27.3%, were allergic in nature. These figures naturally vary with the locality. In Edinburgh, for example, during the year 1939, 1,600 cases presented themselves at the Ear, Nose and Throat Department of the Royal Infirmary with nasal conditions, and of these only 80, or 5%, complained of nasal allergy. This does not /

not take into account, however, those in whom allergy was found incidentally but was not the condition that had led the patient to seek advice. Nevertheless, the figures make one wonder whether allergy is not less common in this country than in America.

The classification of allergic cases into age groups has been reported by several writers. Ferris Smith⁵² (1929) said that 60% of asthma cases occur before the age of 20. Adam² (1925) stated that of 850 cases of asthma 42% began in the first decade of life, while Franklin⁷⁵ (1938) put the figure at 23% in the first decade with an additional 40% having their onset between the ages of 10 and 20. Clarke and Rogers³⁰ (1937) mentioned that 25% of their cases had the onset of their symptoms in childhood. The age grouping at the time of onset compared with that at the time of consultation reveals the interesting fact that there is great delay between the onset of symptoms and the examination by a specialist. This may be accounted for by the pious parental hope that the child "will grow out of it", or by the assiduous blaming of all infantile and childhood nasal trouble on adenoids. Franklin, for example, found that only 13% of his 860 cases consulted him before the age of 20, while 63% sought attention between the ages of 20 and 40. These, perhaps, are the years during which the general public takes a more intelligent interest in personal health.

Vuletić¹⁶⁹, writing in 1934, found a similar state of affairs, 12% of his cases being seen before they were 20 years old, while 70% consulted him between the ages of 20 and 50. Smith¹⁵³ (1932), on the other hand, found in a series of 314 asthmatics that the commonest age groups at onset were 50-60 and 0-10 in that order. This is quite unique and I cannot find any other author who agrees with him. Piness and Miller¹³⁴ (1929), for example, say that the onset is rare after 50, and Heatley and Crowe⁹⁴ (1923) found only 8% arising after the age of 50. My own figures are in accordance with those of the majority of authors. 25% have consulted before the age of 20 and a further 64% were seen between the ages of 20 and 40. The youngest patient was 4, and the oldest 71 years of age.

The following table contrasts my own and Vuletić's figures for ages at consultation with Heatley and Crowe's figures at incidence:-

Ages	CONSULTATION.		INCIDENCE.
	Vuletić	Edinburgh	Heatley and Crowe.
0-10	2%	1.25%	24.1%
11-20	12%	23.75%	19.45%
21-30	20%	42.50%	19.45%
31-40	30%	21.66%	12.9%
41-50	20%	5.42%	16.1%
51-60	12%	3.75%	8.0%
61-70	4%	1.25%	-
71-	-	0.42%	-

The most remarkable thing in the Edinburgh set of figures is the sudden decline in numbers after the age of 40. There has been no accurate account /

account kept of the duration of symptoms before consultation, but the majority of cases had complained for a number of years.

Sexes appear to be fairly equally affected, although some observers note a slight preponderance of females. The Edinburgh figures support this statement, for of 240 allergic cases in the Royal Infirmary 126, or 52.5%, were females and 114 were males. In my own 120 cases there were 61 females and 59 males. In Japanese Hara⁹ (1934) found that the reverse obtained, the proportion of males to females being 5:3.

SYMPTOMATOLOGY.

The classical symptoms of asthma need no repetition here. In many text-books, however, local nasal symptoms are not mentioned. These may or may not be present. When they are elicited, they consist of nasal obstruction, which may be present occasionally or always, and nasal discharge. The discharge may assume a mucoid or purulent character.

The hay fever patient gives a very definite and typical history. During the months of May and June there begins a series of paroxysms of sneezing. These are ushered in by an itching and smarting of the eyelids associated with a tickling sensation felt high up in the nose. There is considerable nasal obstruction and between the sneezes the nose and /

and eyes stream. This nasal discharge contains mucin and so stiffens handkerchiefs. The oedematous mucosa gives rise to a loss of the sense of smell by reason of a blocking of the air current through the upper part of the nose.

Amongst the ocular manifestations are injection and oedema of the conjunctiva with occasionally a dry injected conjunctiva. Infrequently, there is a swelling of the uvula and soft palate with extreme dryness of the mouth. In these cases there is an associated itching of the palate and even the ears. Laryngeal manifestations may include a dry hacking cough with hoarseness. More rarely laryngeal oedema may even be found.

Vasomotor rhinitis, being non-seasonal, is consequently less severe. While hay fever paroxysms last for some minutes, some hours or even days, the sneezing attacks of the more chronic vasomotor disturbance are of very short duration. They may occur every morning on rising from a warm bed into the colder air of the bedroom; they may occur on passing from a cool to a warmer room, or vice versa; they may occur during the dusting of the house or on entering an office that has just been swept. The effects are the same as those of hay fever, but are in miniature. There is not the prostration that occurs with the seasonal variety when the effects may be very exhausting.

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On the other hand, the nasal obstruction is more continual. There are not the months of freedom that are experienced by hay fever patients. The perennial subjects often complain of head colds all the year round - their noses never being clear at all. This stuffiness is worst in the morning and there is often a bad taste in the mouth on waking as a result of mouth-breathing during sleep. Anosmia is often constantly present.

I am convinced, however, that there is an acute variety of vasomotor rhinitis which cannot be called hay fever as it need not occur during the pollinating season. I have had two cases of this - one patient who, in the month of February, sneezed constantly for three days and nights without being able to eat or sleep. The other lady had been sneezing ceaselessly for a whole day at the end of August before coming for advice. These two presented typically allergic noses, but had had no previous allergic manifestations.

Lastly one must not forget that any two or all three manifestations of nasal allergy may co-exist and the symptoms of one may mask those of the other. For example, the chest symptoms of asthma may hide the fact that the patient also suffers from vasomotor rhinitis.

FAMILY HISTORY.

As has been stated, every individual with an allergic /

allergic background is potentially liable to sustain allergic attacks. A hereditary basis is one of Just's¹⁰⁵ (1934) points in distinguishing allergy from anaphylaxis. Such a hereditary tendency must be sought for, but is not easy to ascertain with accuracy. An inadequate history is all too common (Hastings⁹³, 1930) and extreme care must be exercised to approach it from every standpoint. Vaughan¹⁶⁷ (1933) has said that it is insufficient to question as to family history of hay fever, vasomotor rhinitis, asthma and urticaria. One must ask whether any of the patient's antecedents suffered from periodic headaches, eczema, colitis, food upsets, sneezing barrages, intolerance of dust, angioneurotic oedema, drug idiosyncrasy, etc. If all these points are sought after in an intelligent patient Fraenkel's⁶⁴ (1937) 25% and Clarke and Roger's³⁰ (1937) 30% of positive family histories should be exceeded and the figure may well be in the region of 75%. Hara⁹¹ (1934) alone has found that heredity plays no part. His researches were carried out amongst Japanese in America, and it is of interest to repeat here that he alone finds a preponderance of male patients.

LOCAL SIGNS.

Examination of the noses of allergic patients reveals a number of characteristic abnormalities. First of all, the septum is inspected. It may be straight /

straight or it may be deviated to either side, sometimes to a very marked degree resulting in a considerable amount of nasal obstruction.

The mucous membrane is next examined. Typically it is paler than normal, although this is not invariably the case. It may appear quite normal - as, for example, in the symptomless period of hay fever subjects - or, if the subject has a cold, it may appear congested.

The submucosal layer is best studied at the anterior end of the inferior turbinate. Here there is an aggregation of erectile tissue. A cotton-wool-tipped probe moistened with 10% cocaine hydrochloride applied to this area will produce a marked retraction of allergic mucous membrane. Also, if unshrunk mucosa is probed, the elastic oedema will be felt, and pitting on pressure may even be elicited.

The inferior turbinates may be of normal size but typically they are enlarged, and covered with greyish smooth mucous membrane which is shining as a result of its surface film of mucus. The turbinates may appear a dull dead white colour with no covering mucus, and in that case the mucosa is found to be of the squamous type. Normal healthy turbinates are found in some cases of asthma and in the off-season of hay fever subjects. Atrophy is occasionally found in some cases who have had operative interference.

The /

The middle turbinates may or may not be enlarged and covered with a pale grey mucous membrane. In some cases (7% in my series) there is a polypoidal fringe on the free margin of the middle turbinate. Polypi may be seen in all stages of growth, from minute ones just discernible in the middle meatus to larger ones filling the nasal cavities. These polypi also retract markedly when cocaine is applied to them. The figures of polypoidal growth in the series of cases from which I quote are noticeably smaller than those of the majority of authorities. I have found polypi or polypoidal middle turbinates in 11.7% of the cases. James¹⁰² (1933) found polypi in 10% of 125 asthmatics. Higher percentages, however, were found by Kelley¹⁰⁹ (1936), 23%; Stout¹⁵⁸ (1927), 24%; and Duke⁴⁶ (1927) 24%, who notes that polypi are less frequent in seasonal cases. Hansel⁸⁶ (1930) goes even further and says that polypi are never found in hay fever cases - a finding which agrees with this present series. Kern and Schenck¹¹¹ (1933) give no actual figures but say that the incidence of mucous polypi is strikingly high in allergy. Weille¹⁷⁶ (1936) reports 211 cases of polypi in 500 asthmatics. Other figures for the incidence of polypi in allergy are given by Bray¹⁹ (1937) in his "Recent Advances in Allergy". In this he quotes Becker who noted 9 cases of asthma in 360 cases of nasal polypi; Hering who reported

200 cases of polypi with but 7 asthmatics; and Schmiegelow who found 31 asthmatics in 139 polypi subjects. These figures, however, are in no way comparable with the percentages quoted above and merely indicate that allergic polypi are much less frequent than infective ones.

The presence of any infection in the nose or sinuses tends to modify the appearances. Pus or mucopus may replace the mucoid discharge. There may be pus in the middle meatus. The changes occurring in the inferior turbinates as a result of infection are no less interesting and are, to my mind, the crucial points in deciding the form of treatment to be employed. The turbinate may be so overgrown from chronic rhinitis as to have an actual hypertrophic fringe along its free margin. The degree of hypertrophy is ascertained by the amount of retraction produced by cocaine, the two being in inverse proportion to each other.

Posteriorly one may see blanched mucous membrane covering the posterior ends of the turbinates. Polypi or pus may be seen. The presence of any hypertrophic changes in the inferior turbinate will be shown by an enlargement of its posterior end. This is a more delicate guide to hypertrophy than is enlargement of the anterior end, since the size of the posterior end of the inferior turbinate is more constant in health.

An analysis of the findings at examination of the 240 cases in the series reveals the following facts:-

<u>Mucous membrane</u>	<u>Cases</u>	<u>Percentage</u>
Allergy	201	83.76%
Normal	13	5.42%
Atrophy	6	2.50%
Congestion	4	1.65%
Allergy and atrophy	2	0.83%
Hypertrophy	1	0.42%
Not stated	13	5.42%
	<u>240</u>	<u>100.00%</u>

Polypus formation

Polypi	10
Polypoid middle turbinates	17
Choanal polypus	1
No polypi	212
	<u>240</u>

X-rays

Clear	75
One opaque antrum	6
Two opaque antra	6
Thickened mucosa	4
Polypus in antrum	1
No X-rays	148
	<u>240</u>

In my own personal cases I found the following facts in relation to the nasopharynx:-

Enlarged posterior ends	38
Normal posterior ends	70
No notes	12
	<u>120</u>

Two other nasal features have been described in the literature. Just¹⁰⁵, speaking at the B.M.A. meeting at Bournemouth in 1934, stated that many allergics have skin cracks round the external nares. No cure of the allergy results, he says, until these cracks /

cracks are healed. Furthermore, they are all staphylococcal in nature and Just wonders whether there is any reason to suppose that they denote a bacterial allergy. More probably the cracks are caused by the constant rhinorrhoea and the staphylococci are those usually associated with skin infections.

Duke⁴⁸, in 1930, noted a characteristic facial change commonly found in children with perennial allergy. It consists of a depression at each side of the nose in the region of the ethmoidal cells, and is due to a lack of development of these cells from deficient aeration resulting from the oedematous allergic mucous membrane.

I have noted in a number of cases in this series, but more particularly in puny, undernourished children with allergic turbinates, a small pale heaping-up of the mucosa in the floor of the nose just at the level of the anterior end of the inferior turbinate. It is by no means a constant finding but I have never seen it without some signs of pallor of the turbinates. I cannot offer any explanation for its presence in this particular situation.

FURTHER INVESTIGATIONS.

These are undertaken as in the course of a routine investigation of any nasal case. The oropharynx and nasopharynx are examined carefully, and /

and the teeth are searched for dental caries.

The maxillary and frontal sinuses are examined by transillumination, and all the sinuses are X-rayed for the presence of infection. X-rays should be both straight films and with iodised oil in the sinuses (Stout¹⁵⁹, 1930). The results of such an examination are variously interpreted and reported. There is an extraordinary divergence of opinion on the question of how great a part is played by sinusitis in allergy. To me, it seems a perfectly rational supposition that any vasomotor oedema of the lining mucosa of the nose will be shown also as an oedema of the mucous membrane lining the sinuses. The mucosa of the sinuses is continuous through the ostia with that of the nasal cavities. Therefore any case found to have sodden oedematous inferior turbinates will be reported by the radiologist as having a thickened mucous membrane lining in the sinuses. If one takes such a report on its face value and considers it as denoting sinus pathology, there is an absurdly high percentage of "infected" sinuses in a series of allergic cases. The more rational view has been taken by Baum⁹ (1932), who blames misinterpretation for many futile attempts at curing allergy by sinus surgery; by Mullin¹²⁷ (1932) and by Cohen³⁴ (1935). The most convincing demonstration of this rational view was made by Proetz who in 1930 showed to the American Laryngological /

logical Association a case whose previously normal antral mucous membrane was seen by X-ray to become thickened in a few hours after the injection of 40% poppy-seed oil. This was associated with an attack of asthma and the thickening was so great as almost to obliterate the cavity. He¹³⁷ (1930) is of the opinion that a single X-ray showing thickened membrane is not sufficient grounds for operation.

Dennis⁴¹ (1924) found that in 47 cases of "proved" maxillary sinus infection the X-rays in some were misleading as seen at later radical antrum operation. Sewall¹⁴⁷ (1935) is of the opinion that the oedematous state "has been exaggerated to explain the evanescent shadows on the X-ray film. It is obviously impossible", he says, "for normal mucous membrane, which is as thin as cigarette paper, to become 1 or 2cm. thick without the time element essential for hypertrophy of the tissues". He explains the shadows by inspissated pads of mucus. In that case one would expect to obtain mucus on diagnostic proof puncture - a result which is not in accordance with my findings.

On the other hand, the advocates of sinus surgery quote extremely high percentages of infected sinuses. For example, Ferris Smith¹⁵² (1929) found 73% of cases of asthma had sinusitis - a percentage which rose to 82% when radiopaque oil was used. Kern and Donnelly¹¹⁰ (1932) found 80.5% of 200 asthmatics /

asthmatics had sinus infection. Kelley¹⁰⁹ in 1936 gave his figure as 89% of 100 asthmatics, while Cooke and Grove's³⁷ (1935) percentage in 120 cases of asthma was 92% infected sinuses. Weille¹⁷⁶ (1936) in his series of 500 asthmatic cases found that 316 had sinus infection. Gill-Carey⁸¹ (1930) in this country, found 50% of a series of cases had sinusitis. James¹⁰² (1933), however, is more reasonable in his figures. He found suppuration in 9% of sinuses and catarrhal changes in a further 18% of 125 asthmatics. Bullen²⁶ (1933), too, finds that sinusitis is not a common factor in asthma.

Baum¹⁰ (1934) stated that 148 of his 191 cases of allergy had "pathologic X-rays", but he did not jump to the conclusion that these denoted diseased sinuses. Indeed, he only opened 22 sinuses in his series. Carmody and Greene²⁸ (1929), too, are content to say that "X-rays showed involvement of membranes in varying degrees".

In children there is an even more striking contrast for while Lierle¹⁸ (1926) claimed that paranasal sinus disease was present in every one of a series of 20 cases of asthma in children, Bray¹⁹ (1937) says that less than 1% of allergic children have nasal pathology.

In contrast to this mass of material in favour of the presence of sinus infection, my own figures seem rather absurd. In 148 of the 240 cases no X-rays /

X-rays were thought necessary. Of the 92 X-rays taken, 75 were negative, 4 showed thickened lining, 6 showed one opaque antrum, 6 showed two opaque antra, and 1 showed an antral polypus. Furthermore, of the 12 cases which were found to have opaque antra, 11 were washed out and, of these, 9 gave clear returns. I had thus 3 cases of proved antral infection in the whole series - the two positive to proof puncture and the one with the antral polypus!

How are these findings to be explained? By the blind acceptance by some American writers of the radiologist's report? I would suggest that a maxillary sinus may be deemed unhealthy in a case of allergy only if (i) the sinus shows polypoid formation on X-ray examination, if (ii) the sinuses show inequality - one being opaque and the other clear or thickened, or if (iii) the sinuses show repeated mucous membrane thickening in the absence of any such oedema in the nasal cavities. Even then the sinus should not be definitely labelled unhealthy until pus or mucopus has been washed out of it at proof puncture. It is rather noticeable that no acceptable criteria for the diagnosis of sinusitis are given by many who quote high percentages of its incidence.

SKIN TESTING.

In all the reports in American literature of investigation into allergic cases reference is made to /

to the fact that, after a complete examination of the nose and throat, the patient is referred to the allergist for skin testing. I am afraid that I have no personal figures of this form of investigation. The cases seen in the Ear, Nose and Throat Department of the Edinburgh Royal Infirmary are not skin tested unless they have previously undergone a complete medical overhaul.

The tests which are employed are the scratch test and the intradermal test. The latter is more accurate and, apparently, equally easy to carry out. Many of the writers found that a positive reaction was obtained by this method in cases in which the scratch test had failed (Cohen³⁴, 1935, Fox and Harned⁶³, 1938, etc.). The older scratch method and its many negative reactions may have led to Mullin's¹²⁷ (1932) conclusion that although the nose and bronchi were sensitive to proteins in all cases, the skin might not be. Yet Stevens¹⁵⁶ (1934) is of the opinion that lung mucosa is insensitive to feathers, epidermals, etc.

As far as results are concerned, Fraenkel⁶⁴ (1937) found that of 522 asthmatics, 252 were sensitive to house dust, 199 reacted to feathers, 84 to moulds, 108 to bacteria, 42 to animal fur and 55 to other allergens. Smith¹⁵³ (1932) quotes the following order of frequency in 314 cases of asthma, feathers (106), hair (58), pollens (50) and vegetables /

vegetables (37). He also found that only one-tenth of his cases were sensitive to one protein, while half the cases reacted to more than five proteins. Clarke and Rogers³⁰ (1937) in a series of 162 cases found 51% showing a positive reaction to intradermal injections of inhalants. House dust accounted for 75, feathers for 21 and orris root for 14.

Eyermann has written many articles on food allergy. In 1928 he⁵⁷ stated that food allergy might be present with negative skin reactions. In 1930 he⁵⁸ reported the results of 95 cases of food allergy. Of these, he found 30 sensitive to wheat, 24 to egg, 17 to milk, 15 to chocolate, 12 to string bean, 11 to potato, 9 to peas, 8 to salmon, and 7 to tomato. Again in 1938 he⁵⁹ found that the commonest foods eaten were those which most frequently caused allergy.

Rudolph and Cohen¹⁴³ (1934) finding 8% of negative skin tests in a series of 500 nasal allergic cases recommended a nasal mucosal test as an additional test to the intradermal skin test. This test is also advocated by Dean and his co-workers⁴⁰ (1935).

CYTOLOGY AND BIOCHEMISTRY.

One of the most characteristic and constant findings in allergy is the presence of numbers of eosinophils in the blood, nasal lining and nasal secretions. Its presence was noted by Gollasch
fifty /

fifty years ago. Fraenkel⁶⁴ (1937) in a survey of 522 asthmatics, found an eosinophilia of over 4% in 221 of them. Coates and Ersner³² (1930), commenting on the presence of eosinophils in the nasal tissues, wonder whether it is due to protein disturbance, lessened ciliary motility or an allergic response to stimuli. Finck⁶⁰ (1927) made the interesting observation that in the presence of infection eosinophilia disappeared and a polymorph leucocytosis took its place. Kahn and Stout¹⁰⁷ (1932) believe that a routine nasal smear is of great diagnostic value. The presence of eosinophils in the blood has been reported by many workers including Brown²⁰ (1932) and Walsh and Lindsay¹⁷¹ (1934).

Another feature in the blood is the lowering of the blood calcium. This is not invariably found although many people employ calcium extensively in their treatment of allergy. Brown, for example, quotes a calcium deficiency in 37% of cases while Lierle¹¹⁸ (1926) says that the blood calcium varies within limits of 10.4mgm.% - 11.5mgm.%. The ~~phosphorus~~^{potassium} content is normal or slightly reduced so that there may be a slight upset of the ~~phosphorus~~^{potassium}/calcium ratio. Sugar estimation gives normal results and chlorides vary from 0.475gm.% to 0.531gm.%. The pH lies between 7.30 and 7.38.

Brown²⁰ (1932) showed by determination of the basal metabolic rate that some degree of hypothyroidism /

thyroidism is present in these cases.

In 50% of cases occurring in children there was polyuria, and indican was found in many of them (Lierle¹⁸, 1926).

Credit is due to Buhrmester for her work on the biochemistry of nasal secretion. In 1933²³ and in 1935²⁴ she worked out its composition as follows:-

	Water	Solid	Ash	Protein	Ash in solid	Calcium mgm. %	Sodium mgm. %	Potassium mgm. %
Allergy	96.90%	3.10%	1.20%	1.90%	47.80%	11.3	291	79
Infection	90.10%	9.91%	1.12%	8.79%	10.40%	8.9	272	94
	Viscosity	pH	Potassium mgm. %	Character	Cytology	Bacteriology		
Allergy	1.12-1.8 Greater if polypi present	7.11-8.11	62-525	Clear Opalescent Few pale flakes	Eosinophils Neutrophils Bacteria	No growth		
Infection	1.4-3.89	5.96-7.76	124-3306	Pus	The above + Epithelial cells Fibrin Monocytes Lymphocytes	Varies		

These results are of more interest perhaps to the biochemist than to the clinician, but the presence or absence of eosinophils and of sugar is of diagnostic importance in the differentiation between rhinorrhoeas of allergic and cerebro-spinal origin.

The /

The cytology of the nasal secretions was mentioned by Eyer mann⁵⁶ in 1927, and he found that polymorph neutrophils, eosinophils with pale, bilobed nuclei, epithelial cells with large oval nuclei, and occasionally mononuclear phagocytes were present. He said that 72% of allergic cases showed eosinophils in their nasal secretion; of these approximately equal numbers had many, several, and few such cells, while in non-allergics only 9% showed eosinophils.

Hume¹⁰⁰, writing in 1936, concluded that polymorphs in excess in the nasal smears denoted acute infection, lymphocytes meant chronic infection, and eosinophils in greater numbers than 5% showed allergy. Cowie and Jiminez³⁸, also in 1936, made 92 comparative, simultaneous blood and nasal films, and concluded that the results showed no similarity whatever. The eosinophil count was most marked in those sensitive to epiderms and was reduced by the presence of infection.

Eosinophils, too, are found in smears made from nasal polypi. Walsh and Lindsay¹¹ (1934) divide polypi into two types depending upon their eosinophil content. In those with high eosinophil content the polypi are always bilateral, and blood eosinophilia is very frequently found. This finding has been confirmed by Kern and Schenck¹² (1934).

HISTOPATHOLOGY.

The usual description of the microscopic appearances of normal nasal mucosa is that the lining epithelium is of the ciliated columnar type. Between the columnar cells are some goblet cells and the openings of mucous glands. These columnar cells lie on a well-defined basement membrane. Below this there is a "matrix of collagenous fibres" (Munro Cameron²⁷, 1935). In this submucous layer or tunica propria there are numerous glands and blood vessels in the deep part. Deeper still is a denser, non-glandular layer of compact fibrils. In this layer are some fibroblasts and mononuclear cells. If such a description were accurate for all parts of the nose, the allergic abnormalities would be easy to determine. Unfortunately, such is not the case. In a most excellent paper Hollender and Fabricant⁹⁶ (1938) point out the difficulty of evaluating normal mucous membrane. Numerous observers have shown that it may assume the form of ciliated columnar, stratified ciliated, cuboidal, stratified cuboidal and transitional squamous epithelium. The areas at the anterior end of the nose exhibit little ciliary activity which, as Hollender and Fabricant observe, "is not surprising considering that the mucous membrane is exposed to a continuous bombardment of various factors". Not only that, but different biopsies from the same nose may exhibit divergent results./

results.

I have found that more typical sections of nasal mucous membrane are to be obtained from the inferior margin of the middle turbinate, as the inferior turbinate tends to be deficient of ciliae at its anterior end. Hollender and Fabricant's paper supports this and mentions that in the anterior end of the middle turbinate, and in the anterior end and free margin of the inferior turbinate low cuboidal and squamous epithelia tend to replace the ciliated columnar cells found elsewhere.

Probably the most exhaustive study of the microscopic appearances in allergy has been made by Weille¹⁷⁴ (1930), though the contributions by Munro Cameron²⁷ (1935) and Finck⁶⁰ (1927) must also be mentioned.

The epithelium is found to be typically of the pseudostratified type with metaplasia to columnar, cuboidal or stratified squamous. Distended goblet cells are often seen. In some cases there is almost total absence of epithelium. The basement membrane is thickened and in some parts this is very marked. It may show vacuolation, and send finger-like processes into the tunica propria. In some cases it has lost its elastic appearance and has become hyaline.

The tunica propria varies widely. There is some increase in density around the blood vessels, but /

but not so much round the glands. The connective tissue is loose under the basement membrane. Oedema is very marked and is generally regarded as a universal finding, although Hollender and Fabricant only found oedema in 54 of the 160 sections examined.

The vessels vary in vascularity. Usually the bigger vessels lie deep and smaller vessels run out towards the basement membrane where they split into a network. The lining acini of the glands are frequently dilated.

As to infiltrating cells, the majority of observers report the predominance of eosinophils. Weille, however, remarked that plasma cells and lymphocytes were twice as common as eosinophils. He found that the lymphocyte was the commonest cell. Cameron divides asthmatic cases into four groups - (i) in which polymorphs predominate; this is the rarest finding and the appearance differs in no way from acute inflammation: (ii) in which mononuclears predominate; the appearances are those of a chronic catarrh: (iii) in which eosinophils predominate; this is found in status asthmaticus and acute hay fever: (iv) in which eosinophils and plasma cells are equal; this is the commonest condition, and represents the quiescent state of (iii), which is second in frequency.

Murphy¹²⁸ (1931) induced anaphylaxis into guinea pigs whose nasal mucosa normally resembles that of man. /

man. He found microscopically distended goblet cells, eosinophilia, dilated blood vessels and small petechial haemorrhages below the basement membrane. There were also endothelial changes of a fatty nature, and some arteriolar spasm. In other words, the changes closely resemble those found in allergy.

DIFFERENTIAL DIAGNOSIS.

The diagnosis of asthma is usually made by the physician or general practitioner who refers the case for investigation of the nose and sinuses with a view to finding the cause of the asthma. An allergic asthma due to nasal allergy can be diagnosed by a consideration of the history together with an examination of the nose on the lines I have indicated. A careful search must also be made for evidence of sinus infection, for a person may be sensitised to the products of a septic focus without any marked allergic manifestations in the nose. Where facilities for skin testing exist this must be carried out, as it yields more accurate information about the causal protein than does the personal history of the patient. Yet in some instances the patient is aware that a certain food, or a certain locality, will produce an asthmatic attack.

Hay fever is diagnosed by its periodicity, occurring only during each pollinating season. This season usually starts in May or June, but varies according to the geographical situation of the patient's /

patient's home. It begins approximately at the same time each year. During the season the patient suffers from typical attacks ushered in by an itching of the nose or eyes. Then follows a violent burst of sneezing and rhinorrhoea which lasts for a variable time, and leaves the patient in a state of nervous and physical exhaustion of varying intensity. This nervous element frequently takes command and leads to apprehension of each ensuing attack and season.

Vasomotor rhinitis, however, exhibits no such periodicity or acuteness. There are shorter attacks of sneezing, but these may take place at any season of the year. There tends to be a more or less constant nasal obstruction and rhinorrhoea. There is frequently a complaint of recurring head colds present both summer and winter.

Forman⁶² (1934) made an exhaustive study of the differential diagnosis of allergic conditions, which he divides into:-

- (i) Atopic coryza - which he recognises by
 - (a) family history of asthma, hay fever, etc.
 - (b) personal history of asthma, hay fever, etc.
 - (c) eosinophilia of blood and nasal discharge.
 - (d) positive skin reaction.
- (ii) Bacterial allergy - diagnosed by
 - (a) eliminating atopic coryza.
 - (b) history of infection and demonstration of focus.
 - (c) /

(c) delayed cutaneous reaction to injection with offending bacteria.

(iii) Contact allergic coryza occurring in any person at any time in the absence of inheritance and antibodies. It is recognised by

(a) eliminating atopy.

(b) history of exposure.

(c) identifying offending substance by a test application to the nasal mucosa of suspected substances.

(d) relief by avoidance of offending substance.

(iv) Physical allergic coryza - the results of effects of heat, cold, light and other physical agents. It is distinguished by

(a) eliminating other forms of allergy.

(b) history.

(c) production of allergy by exhibiting offending agent.

(d) relief of allergy by avoidance.

Brown²⁰, (1932), who coined an adaptation of Chevalier Jackson's famous "all is not asthma that wheezes" in the phrase "all is not hay fever that sneezes", diagnoses hay fever from recurrent head colds, sinus infection, nasal trouble from reflex or mechanical stimulation and cerebro-spinal rhinorrhoea. In this last condition the feeling of pressure in the head is relieved by a sudden onset of a watery nasal discharge. The diagnostic characteristics /

characteristics of the discharge are the absence of mucin - as is seen from the fact that the discharge does not stiffen handkerchiefs; and the presence of sugar - as is seen by reduction of the discharge on boiling with Fehling's solution.

Just¹⁰⁵ (1934) distinguishes allergy from anaphylaxis by the following facts - (i) allergy is frequently inherited while anaphylaxis is not (ii) allergy appears the first time a person comes into contact with the sensitising substance, while this is not true in anaphylaxis (iii) anaphylaxis is transmitted passively to animals while allergy is not, and (iv) the symptomatology is different.

TREATMENT.

The treatment of nasal allergy divides itself into general methods; desensitisation; interruption of naso-pulmonary reflex by cautery, injection, or ionisation; and sinus surgery.

General Methods.

St. Clair Thomson¹⁶⁰, writing in 1923, says "the history of the treatment of hay fever, spasmodic rhinitis and nasal hydrorrhoea is not very interesting. Most of our patients run the gamut of various intra-nasal operations and applications, including the galvano-cautery, hot air and resection of nerves, with symptomatic treatment by belladonna, strychnine, and so forth. One cannot help wondering how much of the benefit - when there was any - was due to suggestion" /

suggestion". Brown Kelly²², 1925, stressed the fact that constitutional treatment is of first importance - nervine tonics, quinine, arsenic, strychnine, and phosphorus. He advised the physician to allay mental disquietude, and dismisses vasomotor rhinitis as "a functional disease which passes off sooner or later, but is liable to recur". Such general methods are indispensable, but, in the light of our present knowledge, some further line of treatment is necessary. We cannot content ourselves with regarding the condition as purely functional. The allergic basis must receive attention.

Local applications to the nose in the form of sprays are advocated by Brown²⁰, (1932), who uses 1% of ephedrine in liquid petrolatum; and Tobey¹⁶¹ (1930) who advocates epinephrine locally. These have purely a vaso-constrictive action and are in no way curative.

Calcium therapy is based on the questionable assumption that blood calcium is lowered. It is recommended by Vuletić¹⁶⁹ (1934) (calcium chloride), Brown²⁰ (1932) (calcium lactate gr. V or calcium gluconate gr. XXV t.i.d.), Adam³ (1937) (calcium lactate or gluconate) and Huber and Harsch⁹⁹ (1934) (calcium gluconate gr.120 daily). The latter authorities also suggest the use of urea nitrate with which they claim relief in 30% of cases.

Sodium /

Sodium iodide therapy is mentioned by Ramirez⁴⁴ (1938), who gives up to 250cc. of a 4% solution intravenously, which method he considers better than the oral administration recommended by Tobey. No satisfactory explanation is offered for the therapeutic use of either urea nitrate or sodium iodide and treatment by these salts is not widely employed.

Mullin²⁷ (1932) has said that "every allergist should have a sufficient knowledge of botany to be able to advise his patients how, when, and where to avoid wind-blown pollens". Those who have not this knowledge, however, may resort to Vuletic's dictum - send the patient to the seaside or the mountains and get him to wear tight goggles or a mask. Biedermann¹⁶ (quoted in the 1937 Year Book of Eye, Ear and Throat) has devised a mask rather like a civilian A.R.P. gas mask, but with a tight nose-piece instead of the goggles. This mask contains a battery with the poles attached each to a fine mesh. Between the two meshes is a filter which can be changed daily. This ingenious, if ugly, contraption is said to prevent any pollen being inhaled. A somewhat similar mask has been described by Fraenkel⁶⁴ (1937).

Dietetic treatment is advised by Adam³ (1937), who says that the following regime will cure vasomotor rhinitis: (i) stop all milk (ii) induce the patient to lead an open-air life (iii) give calcium gluconate or lactate with cod liver oil and malt (iv) prescribe a /

a weekly mercurial. Cohen and Rudolph³⁵ (1931) make up a diet that is free from any proteins giving positive intradermal tests. With this they claim 49% cures and 34% great improvements. The 17% of failures were due to (a) patients not following the diet (b) patients being unable to afford the diet or (c) patients having a sensitivity which could not be avoided. Eyermann⁵⁸ (1930) also treats his cases dietetically on the same lines.

On a similar basis what may be described as an "avoidance" treatment can be instituted. Where a food is causing allergy, and is avoidable, it should not be eaten. In the same way a geographical change may avoid any specific pollen. Orris root - which is used in the manufacture of toilet articles such as perfumes, powders, tooth paste, face cream, and soaps - can be avoided by choosing products which are free from it, - such as Queen Products. If animals be the cause of the allergy they must be done without, and, similarly, any drugs causing idiosyncrasy must not be taken. Feather pillows should be avoided if they produce any sneezing effects. Such avoidance therapy is recommended by Tobey⁶¹ (1930), Brown²⁰ (1932), and Clarke and Rogers³⁰ (1937).

Where avoidance is impossible on account of the nature or multiplicity of the offending proteins, desensitisation of a specific or non-specific nature may be resorted to. In hay fever subjects a specific /

specific desensitisation can be obtained by injecting increasing doses of pollen extracts (Emerson⁵⁵, 1929, Piness and Miller¹³⁵, 1930, et al.). Piness¹³², writing in 1925, claimed 23% complete cures in hay fever by means of pre-seasonal immunisation. For vasomotor rhinitis desensitisation may be employed, and is probably the method of choice. Alden⁵ (1937) believes it to be the method of choice for hay fever as well. Generally speaking, good results are obtained by its use (Stein¹⁵⁵, 1923, Tobey¹⁶¹, 1930, Vuletić¹⁶⁹, 1934, Furstenberg and Gay⁷⁹, 1937, etc.). Clarke and Rogers³⁰ (1937) treat their cases who have a positive skin reaction to inhalants with graduated injections of a solution of dust and orris root. The doses are given weekly until the patient is clinically free, and then monthly for a year. Stier and Hollister¹⁵⁷ are reported in the 1937 Eye, Ear and Throat Year Book as using pollen extract orally. They obtain 78% of satisfactory results by giving graduated doses varying from m.ii-iii of a 1/100,000 solution every 2-3 days to a drop or two of a 1/100 solution daily. Francis⁷³ (1938) has tried intranasal spraying of pollen after cautery.

Should one imagine that frequently there might be serious reactions as a result of these desensitising injections, Furstenberg and Gay⁷⁹ (1937) report only 87 reactions out of 43,771 therapeutic injections /

injections of allergens.

Lastly, an autogenous vaccine may be used. It may be taken from the nose or the nasopharynx. Clarke and Rogers use it for their patients who have a negative skin reaction, and it has also been successfully employed by Touart¹⁶⁴ (1925) and Coates³¹ (1926).

Intranasal tamponage has not many supporters. Argyrol packs in the ethmoidal area are used by Dowling⁴³ (1925) who popularised them to such an extent that they were known in America as "Dowling's tampons". James¹⁰² (1933) also uses argyrol tampons applied between the middle turbinate and the septum. In 125 cases of asthma thus treated he claims to have cured 28% and greatly improved 63%. There was no change in 5% and the patients were worse in 4%. Carmody and Greene²⁸ (1929) treated some of their cases with 20% ichthyol in glycerine tampons.

Bernheimer and Cutler¹⁴ (1932) report the effects of irradiation on 40 cases of vasomotor rhinitis of which 11 had positive skin tests but no benefit from treatment, and 29 had had previous nasal operations with no effect. 50mgm. radium is left in a cocainised nose for two hours. There is erythema and complete nasal obstruction for 3-8 weeks. This slowly resolves and a healthy pink mucosa is left. The sneezing and oedema disappear. They found no bad effects. All the cases improved and none /

none of them had any recurrence within six months. Hernaman-Johnson⁹⁵ stated in 1937 that X-rays to the chest will relieve many asthmatics. The X-ray treatment of asthma is also discussed by Maytum and Leddy¹²⁵ (1939).

Interruption of the Naso-pulmonary Reflex.

Consideration must next be given to the methods of interrupting the naso-pulmonary reflex or otherwise producing a hyposensitivity of the nasal mucous membrane. An injection of alcohol or other sclerosing substance into the spheno-palatine ganglion will produce an effective block to afferent impulses from the nose. It has been advocated by Stein¹⁵⁵ (1923), Coates³¹ (1926), Ruskin¹⁴⁵ (1930), and Walsh¹⁷⁰ (1932) amongst others. Huber and Harsch⁹⁹ (1934) are of the opinion that relief is only temporary, but Walsh quotes the following results in 90 cases - 9% failed due to faulty technique, 30% free for 1-6 months, 31% symptomless for 6-12 months and 30% free for more than a year. The operation is a difficult one and requires considerable practice. Ruskin¹⁴⁴ (1925) describes three approaches to the ganglion (i) from the spheno-maxillary fossa (as used by dentists) (ii) via the spheno-palatine foramen (suggested by Sluder but requiring a special needle) and (iii) upwards through the posterior palatine canal guided by the large palatine branch to the ganglion. Hansel⁸⁵ (1924) used 15-20% silver nitrate /

nitrate to block the sphenopalatine ganglion. My objections to these procedures are their difficulty, and the fact that no blocking of the anterior ethmoidal nerves is obtained. These nerves supply the upper and anterior part of the nasal cavity and thus are of some considerable importance in the conduction of afferent impulses.

A. Francis⁶⁵, in 1902, astonished his British listeners by describing a new method of treating asthma which he had discovered quite by chance. It was to cauterise lightly certain sensitive areas in the nose, called "trigger" areas. These areas have been defined in a later article by C. Francis⁷² (1934) as (i) the anterior part of the septum (ii) the superior margin of the inferior turbinate and (iii) the anterior margin of the middle turbinate. Francis wrote of his technique in many subsequent articles^{66,67,68,69,70}. A. Francis' figures were 224 (55%) cases cured and 123 (31%) greatly improved in a series of 402 asthmatics. Rowe¹⁴² (1938) is another advocate of cauterisation, and C. Francis⁷² (1934) gives his results as 74% cured or very much improved and only 4% of failures.

Spivacke¹⁵⁴ (1933), Palmer¹²⁹ (1935) and Lewy¹¹⁷ (1937) also cauterise the mucous membrane, but do it much more extensively. The former two men paint pure carbolic, and the latter resorcinol, over the entire surface of the nasal mucosa. In Spivacke's series of /

of 16 cases, 10 had complete and almost immediate relief. This is, however, a form of treatment that does not commend itself to me. It is much too drastic, and the mucosa and submucosa must suffer very considerable and perhaps irreparable damage.

In order to reduce the size of the turbinates attempts have been made to introduce a sclerosing fluid submucously. Levine⁶ (1933) uses sodium iodide with traces of free iodine. Vail⁶⁵ (1933) has used 40-60% alcohol which he injects into the anterior end of the inferior turbinate and the septum opposite it. Fishof⁶ (1938) has devised a special needle for injecting sodium morrhuate into the turbinates. He claims that by this method there is no destruction of the mucous layer. The effects of such injections are short-lived and only last for six to eight weeks.

Sinus Surgery, and other Operative Procedures.

Those authorities who quote such high percentages of sinusitis in nasal allergy find that most of these cases occur in asthmatics. It is rational to make an attempt to clear out disease in any of the sinuses, but one should bear in mind that oedematous sinus mucosa may easily simulate chronic sinusitis. As is usual with any proposed form of treatment, there is at first a wave of enthusiasm in favour of the method. Later, the pendulum swings to the opposite extreme, and nobody has a good word to say for the new /

new therapeutic measure. Eventually a mean is reached and a true estimation of the value of the treatment is obtained.

This holds good with respect to sinus surgery in the treatment of asthma. When the surgeons received report after report from the radiologist that their cases showed diseased sinuses they opened up numerous sinuses in an effort to find a cure for their asthmatic cases. To begin with intranasal operations were performed, but later, as the results proved to be below expectations, more radical surgery was employed. In an effort to restore normal anatomy in the nose, septa were resected submucously on the slightest pretext.

Later, when these cases that had been operated upon had a recurrence of their symptoms, and when a more rational view was taken of the X-ray appearances, there appeared in the literature a series of articles condemning nasal surgery of any kind for allergy. More recently, however, each case is judged on its own merits. Smith's^{'53} (1932) dictum that asthma "must be treated locally, generally if necessary, and individually always" is now being more universally applied. Repeat X-rays are taken if necessary and a sinus is not operated upon until infection has been demonstrated in it beyond all shadow of doubt. A submucous resection of the septum is not carried out unless there is a definite need for it, and, lastly, the /



the myth that removal of tonsils and adenoids will cure asthma in every case has been exploded (Hansel and Chang,⁹⁰ 1940).

As a doctor's aim in all cases is to put the body into as healthy a state as possible, general methods are undertaken in the form of tonics, dietetic correction, drugs, vitamin therapy, etc. In addition, of course, septic foci must be dealt with. A person whose general health is impaired by septic teeth, unhealthy tonsils or infected sinuses is much more prone to any disease, asthma included, than a person whose teeth, tonsils and sinuses are in a healthy state. Thus I should like to draw a distinction between operations to cure asthma, and operations to place the body in as healthy a state as possible. Unfortunately it is not always possible to find out exactly why many of the operations described were performed. Authors are liable to describe their operations in terms of statistics without any close reference to the actual reasons that prompted them to operate.

In 1904 Macdonald²¹ published the results of his treatment of asthmatic cases as follows:-

<u>Operation</u>	<u>Cases</u>	<u>Cured</u>	<u>Relieved</u>	<u>I.S.Q.</u>	<u>Worse</u>	<u>No record</u>	<u>Still under treatment</u>
Removal of polypi	13	5	6	-	2	-	-
Trimming of turbinates	13	8	1	-	-	3	1
Submucous resection	10	4	3	2	-	1	-
Cautery	<u>43</u>	<u>16</u>	<u>9</u>	<u>4</u>	<u>-</u>	<u>3</u>	<u>11</u>
	<u>79</u>	<u>33</u>	<u>19</u>	<u>6</u>	<u>2</u>	<u>7</u>	<u>12</u>

Tod⁶³, in 1925, reviewed the results of various forms of treatment then in general use at the Royal Infirmary of Edinburgh. Her results are:-

<u>Operation</u>	<u>Cured</u>	<u>Improved</u>	<u>No better</u>	<u>Total</u>
Tonsils & adenoids	6	24	15	45
Removal of adenoids	1	5	8	14
Trimming of turbinates	3	14	10	27
Cautery	3	19	38	60
Submucous resection	5	28	12	45
Removal of polypi	3	10	18	31
Antrum operation	-	-	3	3
Sluder's operation	-	-	3	3

The most interesting part of this table is the fact that only 3 antrum operations and 3 Sluder operations had been carried out, and that all 6 had proved failures. The only other authority who uses the Sluder operation is Dowling⁴³ (1925), and he only uses it before applying his argyrol tampons.

The vast majority of the literature on the subject of sinus surgery again comes from America. The writers who obtain benefit from surgery are nearly all in agreement that greater relief is obtained by radical surgery than by intranasal operations. For example, Fox and Harned⁶³ (1937) performed 50 intranasal ethmoid operations with 16 cures; 40 intranasal ethmoid and double Caldwell-Luc operations with 18 cures; 40 complete exenterations /

exenterations of all sinuses with 16 free for six months to a year and the other 24 free for up to five years. Thus it is seen that the chance of cure increases with the severity of the operation.

Cooke and Grove³⁷ (1935), in a series of 120 cases, also found that the percentage of cures increased if more radical surgery were employed. They found that 70% of their patients who had intranasal operations were better, and that 82% of those who had radical surgery were improved. De Stio⁴² (1936) is probably the most radical of all operators. He subjected 13 asthmatics to a double fronto-ethmoid operation together with a double Caldwell-Luc operation. This unnecessary onslaught on the sinuses resulted in only 3 cures. Perhaps this is just as well, or this brutal method of treatment might be more generally used!

Ferris Smith⁴³ (1929) is another advocate of radical surgery. He thinks that a complete removal would relieve 70-80% of cases of asthma, and quotes the following authorities in support - Lorie's 35 cures from 39 radical ethmoidectomies; Bishop's¹⁷ (1927) 40% cures and 56% improvements from tonsillectomies and nasal operations; and Brown's²¹ (1917) 18 improvements in 27 cases.

Lierle⁴⁴ (1926) operated on 20 children, performing intranasal operations or removing tonsils and adenoids. He found that 17 of them improved, their /

their asthma being greatly relieved. Dennis⁴¹ (1924) reported 19 improvements in 28 asthmatics who had double radical antrum operations under local anaesthesia. Schenck and Kern⁴⁶ (1932) found temporary improvement, lasting on an average for five and a half months, in 83% of 35 cases of asthma who had a double Caldwell-Luc operation. Grove and Cooke⁵³ (1934) find an average of 70% improvements in a series of 247 intranasal and radical antrum operations in 120 asthmatics. Weille¹⁷⁵ (1933) puts the figure at 75% in his cases, but says that they have only a 50% chance of long-continued relief.

In this country Dundas Grant^{52, 53, 54}, in three papers published in 1913, 1927 and 1929, finds the following percentages in nasal surgery - cured 20.8-24.14%, improved 60.3-65.5% and unchanged 10.3-18.9%. He makes no attempt to explain the increased percentage of favourable results reported in his later papers.

Only Coates³¹ (1926) and McGinnis¹²² (1927) advocate a more conservative line of operative treatment. They merely attempt to ensure ventilation of the nose, and to restore normal anatomy as far as possible. C. Francis⁷¹ (1929) put forward the extraordinary view that patients can be relieved of asthma by operation only if they have no idiosyncrasy to aspirin. Those who cannot take aspirin, he says, derive no benefit from /

from operative procedures.

It must not be imagined that all authors are in favour of sinus surgery. There are many articles in the literature deploring unnecessary operations. Duke⁴⁶ (1927), for example, says "the removal of polypi does not remove the cause, and operation on the sinuses rarely relieves the condition except for the time being". Baum⁹ (1932) - as has been mentioned - ridicules the futile attempts to cure asthma by extirpating diseased mucosa. "Not only", he says, "do the asthmatics still wheeze, but the sinuses themselves are not cured and still form polypi". Heatley and Crowe⁹⁴ (1923) also condemn indiscriminate operations. Kahn¹⁰⁶ (1924) says that "it is not to be expected from an operation on the nose that asthma will be at all influenced". Lintz¹²⁰ (1925) is of the opinion that intranasal operation as a cure for asthma is futile. He found that over 30% had no benefit at all from the operation. Piness and Miller¹³³ (1925) found that a series of 834 allergics had 704 operations without relief, there having been no removal of the allergen. They advocate that surgery should be reserved for the removal of septic foci. Moll¹²⁶ (1934) found only 3 of 109 operated patients who were free from asthma for two years. Rackemann and Tobey¹³⁸ (1929) are pessimistic about the efficacy of surgery, and state that only 5% of cases have a permanent relief.

Schenck /

Schenck and Kern¹⁴⁶ (1932), too, are of the opinion that relief is only temporary. Warner and McGregor¹⁷² (1933) obtained only 2 permanent cures in a series of 31 radical antrum operations for asthma.

Emerson⁵⁵ (1929) and Vaughan¹⁶⁶ (1930) are more moderate in their views and state that the results are no better with surgery than without. This is a conclusion that is arrived at also by most investigators into the question of removal of tonsils and adenoids for asthma. Duke⁴⁴ (1926), Stout¹⁵⁸ (1927), Bullen²⁵ (1931) and Bray¹⁹ (1937) all find that the results are the same with and without operation. Bullen used 300 tonsillectomised children and 300 controls, while Bray took his findings from 1,000 cases after operation and 1,000 controls who were advised to have their tonsils removed but did not. Peshkin¹³¹ (1927), in a series of 100 cases, found one improved and three made worse as a result of the operation. The remainder were unaffected.

To my mind, Jay¹⁰³ (1935) and Fox and Harned⁶³ (1937) strike the right note when they emphasise the necessity for a careful selection of cases for operation. Fox and Harned, for example, only operate on those cases who have permanent nasal obstruction or sinus infection. All others are treated non-surgically.

The failures with the tonsil and adenoid operation /

operation are only to be expected. There is a popular belief that any childish ailment can be cured by removal of tonsils and adenoids, and it is probable that many of the cases seen in later life complaining of asthma have had their tonsils and adenoids removed for some vague nasal obstruction, which has been the precursor of asthmatic dyspnoea. Personally, I should never advocate this operation in asthmatics unless the tonsils or adenoids formed a very definite septic focus.

Regarding nasal operations, I think it deplorable that asthmatics, who cannot be considered as good operative risks at the best of times, should be subjected to such extensive procedures as advocated by De Stio and others. Admittedly, a frankly infected sinus should be cleared out - preferably by radical surgery (Potts¹³⁶, 1930) - but a wholesale slaughter of the sinus mucosa seems to me quite unnecessary. In my view operative procedures in the nose should always be minimal, and this should be especially the case where the mucous membrane is universally diseased. Polypi must be removed and the offending ethmoid cells opened up, but this may well be done intranasally. Maxillary antra should be cleared out by the radical, or Caldwell-Luc, operation when the presence of infection has been definitely established. Submucous resections need only be considered where the septum is /

is so grossly deflected as to block one or other side of the nose more or less completely. Frankly hypertrophied turbinates may be lightly trimmed and the cut edges cauterised, or Francis' technique with the cautery may be followed instead.

As my figures show, however, extensive sinus infection or gross polypus formation in asthma appears to be relatively rare in Edinburgh and the need for sinus surgery does not often occur in our cases. Thus a more generally applicable form of treatment is necessary. This is obtained by the use of zinc ionisation.

One form of operative treatment which has everything in its favour is quoted by Bourne (1939). Those cases which develop their asthma following nasal injury with resultant deviation of the septum benefit enormously from submucous resection of the septum.

ZINC IONISATION.

The therapeutic use of a galvanic current was first described by Baber to the Laryngological Society in London in 1898, when he mentioned its use in the treatment of nasal hydrorrhoea. In 1907 Leduc¹⁵ discussed ionic therapy, while in 1919 Friel⁷⁸ described his apparatus for the ionisation treatment of nose and ear cases. He used very weak zinc sulphate solution and employed a current of 15 milliamps. for ten minutes. In 1927 Demetriades advocated /

advocated the use of a weak electric current, zinc electrodes and a calcium electrolyte to obtain relief in seasonal and non-seasonal nasal allergy. In this country Franklin⁷⁴ published in 1931 the results of his six years experience in the zinc ionisation treatment of hay fever. The credit for the popularisation of the treatment in America is due to Warwick¹⁷³, who published his first report in 1934.

The technique of zinc ionisation as used by the St. George's Hospital staff is as follows: the nose is sprayed with 10% cocaine hydrochloride, and then packed with cotton wool soaked in 1% zinc sulphate. Zinc electrodes, covered with wool and zinc sulphate, are applied to the nose. These are attached to the positive pole of a machine generating galvanic current. The negative pole is applied elsewhere on the body. The treatment recommended is given at weekly intervals for three weeks. The first week a dosage of 3 milliamps. is given for 15 minutes; the second week the dose is 4ma. for 15 minutes; and the third week the dose is 5ma. for 15 to 20 minutes. This treatment is preferably given for the three weeks preceding the hay fever season and it is recommended that the treatment be repeated on the succeeding two years.

I followed this technique in its broad principles at first, but later, as I found little benefit from the 3ma. dosage, I reduced the treatment to two applications /

applications, with a week's interval. The dosage the first week is 4ma. and the dosage the second week is 5ma., each being given for 15 minutes. Furthermore, I found it was possible to treat two or even three patients at one time with the Pantostat machine. In this way hay fever patients were able to have more immediate treatment.

The nose is first sprayed to reduce the sensitivity of packing. Otherwise the insertion of wool or gauze into the nose, particularly the ethmoid area, is an exceedingly painful procedure. Care must be taken, however, that the nose is not over-cocainised, or the patient will not be able to feel when the current is too strong, or if an electrolysis burn is being produced.

Next the nose is carefully packed with small pieces of wool wrung out in 1% zinc sulphate solution. These must cover the entire surface mucosa of the nose, and must be in contact with each other so that the current may have uninterrupted passage. Next the electrodes, which are of zinc wire ^{partly} insulated by means of rubber tubing, are applied. The end to be put into the nose is covered with wool soaked in zinc sulphate. If any part of the wire be left uncovered, there is the danger of an electrolysis burn to the vestibule. The other end of each electrode is attached to some form of carrier worn on the forehead and supported by a band /

band round the head, or in the form of a spectacle frame. I have used the latter for some time and found it lighter and more acceptable to the patient than the uncomfortable head-band.

This carrier is connected with the positive pole of the machine, while the negative electrode is placed in a basin of water or saline in which the patient keeps his hand. The generating machine used in the Hospital cases has been a Pantostat run from the mains, while in private cases I have used a dry-cell battery connected through an ammeter. Either produces a satisfactorily steady current, the dry battery outfit being less liable to fluctuation.

The current is now switched on and slowly increased to 4 or 5ma. as is required. Any sudden increase of current renders the patient liable to a mild electric shock. When the desired current is reached it is maintained for the required time and then gradually reduced to zero. The electrodes are now disconnected, and the wool removed from the nose.

During the treatment the patient should experience no unpleasant symptoms at all. If the cocainisation has been properly done there is a feeling of tingling in the nose and, sometimes, in the hand that is connected with the negative pole. The patient also experiences a metallic taste in the mouth. If the cocainisation is too great /

great there are no nasal sensations at all. After the first treatment the patient usually has a mild hay fever attack. There is some sneezing and rhinorrhoea while the eyes may water. One must be careful to warn the patient of such sequelae or further treatment may be avoided. The hay fever attack lasts for some hours, but never in my experience for more than nine to ten hours. Thus a case treated in the morning can be assured of a good night's sleep and may undertake a full day's work on the next day. These after-effects are never experienced following subsequent ionisations, no matter what length of time has elapsed since the previous one.

There are many modifications of this basic technique to be found in the literature. Some people prefer to use a cocaine pack in the nose before applying the electrodes. For reasons given I should tend to condemn this method as being liable to produce damage to the nose as a result of an over-strong current. Others believe that no preliminary anaesthesia is necessary, but I do not feel that adequate apposition of the packs is possible without some surface anaesthesia. It is essential that the zinc-soaked material be accurately placed to ensure that all parts of the nasal cavity are treated.

With regard to the medium for applying the zinc /

zinc to the tissues, I use cotton wool as it is soft, easily moulded to fit any space, and relatively painless. A roll of ribbon gauze will maintain perfect electrical continuity, but it is harder than wool and therefore more painful in the nose. Some people have advocated the use of a jelly containing zinc sulphate. Gale⁶⁰ (1935) goes even further and uses zinc sulphate solution itself. This is allowed to flow gently through the nose with the head held slightly forward. The fluid comes through a glass tube, containing the electrode, and flows into the nose. As it touches the nasopharynx it causes the soft palate to lift up and thus it runs out of the other nostril. Gale keeps his patients sitting in this position for ten to twenty minutes while they have a current of 6-10ma. To my mind, while this overcomes the difficulty of packing round septal spurs, etc., there is no guarantee that the fluid is reaching all parts of the nose.

The strength of the electrolyte also varies considerably. Franklin⁷⁴, in 1931, suggested 1% zinc sulphate. Friel⁷⁸ (1919) had used a solution that was about one-seventh of this strength. I have heard that a solution as strong as 4% zinc sulphate may be employed. Whatever the strength, it is a clinical fact that glycerine should be added as the fluid is thus rendered less painful to the nasal mucosa./

mucosa. The only other authority who followed Demetriades' idea of calcium as an electrolyte is Chajutin, who, in 1933, treated some cases of vasomotor rhinitis with 2% calcium chloride and tin electrodes.

Except Chajutin all authorities use zinc electrodes. Many use pure zinc, but Warwick¹⁷³ (1934), who has experimented a good deal with various methods, finds that the best electrode is an alloy of zinc, tin and cadmium.

For ease of packing, a submucous resection of the septum may be carried out in certain cases. This is an eminently sensible procedure provided the position is explained to the patient, so that he does not imagine that the operation will be curative. The procedure was first recommended by Franklin, and was later endorsed by Warwick, who lets six weeks elapse between operation and ionisation. In this series none of the cases had a submucous resection for this purpose. Such operations as had been carried out were performed as "cures". I have felt that many of the cases would have responded better to ionisation had they had their septa resected first.

As to dosage, this is variously recommended as from 3 milliamps. to 15 milliamps. I venture to think that any current stronger than 7 or 8ma. will not be tolerated by a patient whose nose has not been /

been completely anaesthetised. Unfortunately, the ammeter of the Pantostat only reads up to 5ma. and so the Hospital cases have never had a higher dosage than this. In my private cases, however, I have endeavoured to test out what dosage is possible without pain. By getting the patients to state whenever pain is experienced, I have come to the conclusion that 7 to 8ma. is the uppermost limit that a lightly cocainised nose will endure. A nose that has been over-cocainised, however, will suffer a much higher current without pain, and this may constitute a source of the bad results obtained. It is a question whether the higher milliampère does not produce some destruction of the mucosa or submucosa, and so nullify the results (Shields^{'49}, 1937).

The time of each treatment is ten to fifteen minutes. In some vasomotor rhinitis cases who have repeated ionisations as long as twenty or twenty-five minutes may be given. Warwick believes that 100 milliampère-minutes should be given at each treatment.

After an ionisation treatment there is seen to be a membrane covering the nasal mucosa. This is quite a tough lining and stays in position for three to four days when it disappears. By the end of a week there is often a striking improvement in the appearance of the mucous membrane, the oedematous pallor approaching a normal pinkness. Tobey^{'62} (1935) says "the change in the appearance of the mucous membrane /

membrane is as striking as the relief from symptoms. The mucous membrane takes on the colour of normal healthy lining".

The question is asked by everybody who obtains good results by zinc ionisation, "How does ionisation act?" Friel⁷⁸ (1919), who used the treatment mainly for aural discharge, suggested that ionisation resulted in the production of zinc albuminate on the tissues. Alden⁴ (1935) expresses the more modern view when he says that, when a galvanic current passes between two poles, positively-charged ions pass from the cathode to the anode and are deposited there. Thus, in the human, positively charged zinc ions pass towards the negative pole and so are deposited on the nasal mucous membrane.

Zinc ions are not forced into the tissues. McMahon¹²⁴ (1934) states that Clarke has shown that many therapeutic ions such as silver, iron, magnesium, and arsenic can be introduced through unbroken skin. Lierle and Sage¹⁹ (1932), however, were unable to demonstrate zinc either qualitatively or spectrometrically in the tissues of the ear after ionisation. The zinc ions, then, do not penetrate the mucosa, but produce a mild surface coagulation, as evidenced by the greyish membrane.

Many have seized on this as evidence that ionisation has definite deleterious effects on the nasal mucosa. The chief of these objectors is McMahon /

McMahon¹²⁴ (1934) who, as a result of his experiments on the frontal sinuses of dogs, concludes that there are definite destructive changes in the mucosa. He passed a current of 5ma. through a dog's frontal sinuses filled with 2% zinc sulphate, using a zinc electrode which did not touch the sinus walls. The changes found were "ballooning, fragmentation and complete destruction of the surface epithelium, marked oedema of subepithelial tissues, and extravasation of red blood cells into these tissues from greatly dilated and ruptured capillaries". It was noticed that the adjacent accessory frontal sinuses which were not subject to ionisation showed none of the changes described.

These are very sweeping charges, but one of the obvious questions that one asks is - does 5ma. in a dog correspond to 5ma. in man? If not, then that would lend strength to the view that high ampèrage is harmful to the nasal mucous membrane. Another question is - does not the already swollen mucosa in allergic disease resist ionisation better than normal mucosa, and certainly better than that of healthy dogs?

Hollender and Fabricant⁹⁶ (1938) stress these points and conclude from their work that McMahon's experiments are not applicable to humans. They say that in studying the effects of ionisation one must remember that the treatment is carried out on allergic /

allergic mucous membrane which is pathological, and suggest that many of the so-called effects of ionisation are the same as those found in allergic mucosa. Not infrequently there are less gross pathological changes after ionisation as compared with those before ionisation. This may be due, they say, to repair or to variations in normality.

Alden⁴ (1935) also doubts McMahon's work which, he says, is entirely without scientific basis. When one thinks of the regeneration of mucous membrane in an antrum after its total removal in a Caldwell-Luc operation, he says, one cannot visualise any permanent damage by reason of ionisation. He quotes Knowlton¹³ (1928) and McGregor²³ (1931) as illustrating this regeneration of mucosa after radical antra. Alden concludes that the histological results after zinc ionisation are (i) an intact ciliated epithelium layer (ii) some submucosal fibrosis and (iii) an infiltration of round cells. Bernheimer¹³ (1936) found no marked fibrosis after ionisation, and thought its effects were similar to those of escharotics. Shields¹⁵⁰ (1937), too, finds no fibrosis and no permanent epithelial damage. Alexander⁶ (1936), on the other hand, thinks that the only permanent change is a little fibrosis. From the few specimens I have taken after ionisation, I have only found a slight submucosal fibrosis. There has been no noteworthy change in the epithelium.

It /

It appears, then, that no exact pronouncement can be made as to the histological effects of zinc ionisation until a more accurate knowledge of the microscopical findings in a normal and an allergic nose is obtained. There may be a transient damage to the surface epithelium, caused apparently mechanically by packing and removing the wool as well as by the galvanic current. There is a subepithelial response by fibrosis which tends to shrink down the lining membrane resulting in an increased nasal airway.

That ionisation in no way alters the allergic status of the body has been shown by many writers, among them Dean³⁹ (1935) and Alexander and Alexander⁷ (1935), who found that the skin reaction and the blood eosinophilia did not alter in any way as a result of ionisation.

The results of ionisation, then, are purely local. There is, in successful cases, a relief of symptoms, and the return of the nasal mucous membrane to normal. There is still a potential liability to allergy as is shown by the positive skin tests. Against this, however, there are no disfiguring scars. There is no mental upset. Children can have the treatment as well as adults, though, of course, the dosage is smaller - $2\frac{1}{2}$ -3ma. being sufficient. In a total of 492 ionisation treatments, I have had no adverse sequelae, although some /

some have been reported in the literature, notably the onset of asthma (Parlato¹³⁰, 1936, and House and Gay⁹⁸, 1936). Nor have I found any evidence in support of the criticism that anosmia results from ionisation. Rather is the reverse the result, the patients finding a growing improvement in their sense of smell in consequence of an increased airway in the upper part of the nose. The only contra-indication that I have found is an acute coryza. To ionise in the presence of a rhinitis is to run the risk of an acute sinusitis. Hansel⁸⁷ (1936) has found that maxillary sinusitis may supervene in such cases. Shields¹⁵⁰ (1937) believes that all septic foci should be cleared up before ionisation is started, in order that the best results may be obtained.

Zinc ionisation, or iontophoresis as it is called by many American writers, may be used for any form of nasal allergy - hay fever, asthma or vasomotor rhinitis. Perhaps one might deal with each condition separately and correlate the results at the end.

Hay Fever.

The treatment of hay fever by zinc ionisation was described by Franklin in 1931, when he reported 25 cases all of whom were cured. Clive Shields¹⁴⁸, who was so impressed with Franklin's writing, supported the value of ionisation for hay fever but quoted /

quoted no figures in his article in 1936. In 1937 he reported with Bailey⁸ the results of 243 cases of hay fever, aged 5-77. There was complete relief in 57.6%; considerable relief in 36.0%; some relief in 5% and no relief in 1.4%. Franklin⁷⁵, writing in 1938 on his cases for the previous year, found 9% cured; 35% greatly improved; 46% slightly benefited; 8% not relieved and 2% worse. Again in 1939 he⁷⁶ quotes his 1938 figures as follows - cured 18%; greatly improved 50%; improved 25%; not improved 6% and made worse 1%. These figures are the results of well over 1,000 cases and must therefore be given very considerable emphasis in assessing results. Franklin attributes the improvement in his 1938 figures to (i) a less severe hay fever season (ii) a current of 6-8ma. instead of one of 3-5ma. and (iii) treatment at the beginning of an attack instead of as a prophylactic measure before the season started.

In America, Warwick¹⁷³ (1934) found that in 40 cases, 31 were cured by one ionisation (of 100 milliampère-~~hours~~^{minutes}), seven required two ionisations, while one needed to be ionised thrice. Hurd¹⁰¹, writing in 1935, gives the following results of 521 hay fever cases:-

58%	obtained from	95-100%	improvement		
8.4%	"	"	85-90%	"	} greatly improved
8.2%	"	"	70-80%	"	
3.8%	"	"	60-70%	"	
8.6%	"	"	40-50%	"	
1.5%	"	less than	30%	"	} improved
11.1%	"	no		"	

I find it difficult to understand how he arrives at his percentage of improvement and, for comparison, I shall use his figures thus - cured 58%, greatly improved 20.4%, improved 10.1% and unimproved 11.1%.

As against these apparently excellent figures one must quote the following opinions and figures. House and Gay⁹⁸ (1936) in four cases obtained one improvement, one no better and two worse. Ramirez¹³⁹ (1936) found no improvement in any of 50 cases of hay fever. In the same year he¹⁴⁰ reported a further 100 cases with bad results. The current he used was 10ma. for 10 minutes or 5ma. for 20 minutes. He noted that reactions were more slight with the latter current. Rowe¹⁴² (1938) finds results are no better than those obtained by "simpler and safer methods" (cautery). He adds that discomfort after ionisation is usually great. Bernheimer¹³ (1936) finds that hay fever is unaffected by ionisation, while Alexander⁶ (1936) says that hay fever cases ionised before the season do poorly, but those treated during the season do better. He adds that ionisation "if performed late enough so that the season is over when the effect wears off has all the appearances of a cure".

My own figures are taken from 24 cases, 4 of whom never reported and so no inference can be drawn from them. Of the remaining 20 cases, 10 were cured /

cured, 6 greatly improved, 4 improved and no cases unaffected.

I cannot understand how Ramirez has failed to obtain a single cure in 50 cases of hay fever. With accurate diagnosis, careful packing of the nose and moderate dosage there should be no difficulty at all in obtaining good results. My cases have usually been treated during the season for their first year and pre-seasonally thereafter. It has been suggested that after three years of pre-seasonal ionisation there should be no further recurrence of hay fever.

In my opinion ionisation is of the utmost importance in the treatment of hay fever. At least 50% of cases should be cured by this method and a further 40% should be improved. The cases which obtain no benefit should be negligible if attention is paid to technical details. I incline to the belief, also, that a case should receive treatment after its first hay fever attack each season. In this way one is ionising a nose whose mucous membrane is allergic, and not the normal mucosa of a hay fever patient during the off-season. Also one can more accurately estimate the degree of benefit obtained, as the attack should appear later each year if the treatment is succeeding.

Vasomotor Rhinitis.

The treatment of vasomotor rhinitis follows the principles laid down for the relief of hay fever.

My /

My cases latterly have had two treatments with a week's interval between them. The dosage at the first one has been 4ma. for 15 minutes, and at the second 5ma. for 15 minutes. The cases have then reported back at the end of a month when, if they have had no further trouble, they are told to report at increasing intervals of time. If they have had any nasal obstruction or rhinorrhoea, they have a further 5ma. for 15-20 minutes, and this is repeated at monthly intervals as required. The average number of treatments necessary to obtain a satisfactory result is four. I have treated 56 such cases with 13 (24.1%) cures, 22 (40.7%) great improvements, 10 (18.5%) improvements, and 9 (16.7%) failures. Hurd¹⁰ (1935) in 111 cases gives his results as:-

42.3%	obtained from	95-100%	improvement	
7.2%	"	"	85-90%	"
13.5%	"	"	75-80%	"
2.7%	"	"	60-70%	"
9.0%	"	"	40-50%	"
7.2%	"		less than 30%	"
18.0%	"		no improvement.	"

} greatly improved
} improved

Grouping these as before, I find Hurd's figures to be - cured 42.3%, greatly improved 23.4%, improved 11.7% and unimproved 18.0%.

Alden⁵ (1937) finds vasomotor rhinitis to be greatly improved because ionisation produces a mechanical change in the nasal mucous membrane rendering it less liable to produce vascular or secretory responses. The change is of a fibrotic nature /

nature. Tobey^{'62} (1935) states that his immediate results in vasomotor rhinitis are excellent, while Ramirez^{'39} (1936) found that the vast majority of his 25 vasomotor rhinitis cases were improved.

Among those who find ionisation of no benefit in vasomotor rhinitis are Adam³ (1937), who describes the procedure as futile, and Bernheimer^{'3} (1936), who found only 5% of cases improved. House and Gay^{'98} (1936), in four cases, obtained improvement in one and a worsening in one, the other two being unaffected. Rowe^{'42} (1938) is of the opinion that the results are no better than those obtained with cautery.

Most of the opinion expressed is that zinc ionisation has a much better effect in hay fever than in vasomotor rhinitis. Such has been my own experience in the reported series of cases. In hay fever I have not failed in any single case to obtain some degree of benefit, while nine of my 56 cases of vasomotor rhinitis have been unimproved. In an endeavour to find out why these cases failed, I have scrutinised the case notes carefully and found that six of these failures had enlarged posterior ends of the inferior turbinates.

I have said elsewhere in this paper that enlargement of the posterior ends of the inferior turbinates is a true indication of actual hypertrophy of the nasal mucosa and submucosa. It is not possible /

possible for ionisation to produce the mechanical shrinkage of which Alden speaks in a hypertrophied nasal lining without the presence of oedema.

Ionisation can remove oedema by producing a submucosal fibrosis, but in a true hypertrophy there is an increase of connective tissue only. On this ionisation can have no effect at all. To my mind, therefore, the criterion of whether zinc ionisation will be effective or not depends on the presence or absence of true hypertrophy of the nasal mucosa.

Cocaine hydrochloride should be applied to the inferior turbinates. If they shrink markedly ionisation will result in very considerable improvement; if some shrinkage be obtained and the posterior ends are not enlarged improvement may be looked for; if there be some shrinkage but the posterior ends are enlarged there may be some improvement; if there be no shrinkage and the posterior ends are enlarged there will probably be no improvement.

Asthma.

I have had the privilege of treating a number of cases of asthma who were sensitive to inhalant proteins. They have had the same routine treatment as the vasomotor rhinitis cases. In all, 35 cases have received treatment. Four of these did not report after the treatment was concluded. Of the remaining 31 cases, 10 (32.26%) were cured, 16 (51.61%) /

The remarks regarding turbinate hypertrophy in the vasomotor rhinitis cases hold good for asthmatics. Where true hypertrophy is found, little benefit will be obtained by ionisation alone.

Other Cases.

I have treated four patients by ionisation who had a combination of asthma and hay fever. One of these was cured of both conditions and the other three were greatly improved. In this connection it is of interest to note that Jobson¹⁰⁴ (1937), having failed to obtain any benefit in three cases of this nature, wonders whether such a combination does not mean a bad prognosis. House and Gay⁹⁸ (1936) have treated four similar cases, one with improvement, two unaffected and one made worse.

One case with a mixture of hay fever and vasomotor rhinitis has failed to respond to my treatment by ionisation.

Correlation of Results.

The results I have obtained may be tabulated as follows:-

<u>Condition</u>	<u>Cases</u>	<u>Cures</u>	<u>Greatly improved</u>	<u>Improved</u>	<u>No benefit</u>	<u>Never reported</u>
Vasomotor rhinitis	56	13(24.07%)	22(40.74%)	10(18.52%)	9(16.67%)	2
Asthma	35	10(32.26%)	16(51.61%)	3(7.68%)	2(4.45%)	4
Hay fever	24	10(50.00%)	6(30.00%)	4(20.00%)	-	4
Asthma and hay fever	4	1(25.00%)	3(75.00%)	-	-	-
Hay fever and vasomotor rhinitis	1	-	-	-	1	-
	<u>120</u>	<u>34(30.92%)</u>	<u>47(42.73%)</u>	<u>17(15.45%)</u>	<u>12(10.90%)</u>	<u>10</u>

Of the twelve unsuccessful cases, two have been improved by trimming of the inferior turbinates and removal of the posterior ends. Two more have been cured by subsequent cauterisation. One other was a veterinary student who had no trouble until he began his studies. Another was a lady who was sensitive to dogs and cats, but would not hear of having these animals removed from her house because her children doted on them. I have later heard that she was very much better after a five months' stay in a Nursing Home in which, presumably, her domestic pets were not allowed to roam unrestricted.

Another patient, who worked in a chemical factory, became sensitive to morphia and its derivatives, and was only temporarily relieved by ionisation. The eighth failure subsequently had treatment with ephedrine sprays, calcium gluconate therapy, and finally progesterin with no benefit whatsoever. No improvement was obtained in a further case who had had a previous antrum operation resulting in some atrophy of the nose.

Of the remaining three, one had enlarged posterior ends of the inferior turbinates and these have not yet been removed. A second has a small polypus which has just been removed, while the third is a small child of eleven whose allergic mucosa is now apparently normal, although the mother denies that there has been any real improvement.

Effects of Previous Nasal Operations.

Many of the cases have had some previous nasal interference, which has not resulted in any improvement in the allergic condition. Of these operations, the submucous resection of the nasal septum has been the most efficacious as far as subsequent ionisation is concerned. It allows an easy packing of each side of the nose. The ionisation may be performed as early as six weeks after the operation. Antral operations appear to have a deleterious effect on the nose from the point of view of ionisation. In the antrum operation a partial turbinectomy is usually done, and the resulting fibrosis leads to poor results in ionisation for reasons already mentioned. Similarly a turbinectomy performed alone will give poor results at later ionisation. Removal of polypi, on the other hand, is a good operation as it allows the effects of ionisation to reach the ethmoid cells. The results from ionisation in a nose which has been previously cauterised have been moderately good. I feel, nevertheless, that in some cases cautery has been too deep and the resultant fibrosis too great for ionisation to produce much benefit.

The effects of ionisation in cases with previous nasal interference are:-

<u>Operation</u>	<u>Cases</u>	<u>Cures</u>	<u>Greatly improved</u>	<u>Improved</u>	<u>No benefit</u>	<u>Never reported</u>
Intranasal antrum	3	-	1	-	2	-
Submucous resection	7	1	6	-	-	-
Trimming of turbinates	1	-	-	1	-	-
Removal of polypi	1	1	-	-	-	-
Cautery	14	2	6	3	2	1
Total	<u>26</u>	<u>4</u>	<u>13</u>	<u>4</u>	<u>4</u>	<u>1</u>

RESULTS OF TREATMENT.

The results quoted in the various forms of treatment are all satisfactory. On the whole, about 80% of cases are either cured or greatly benefited. To give a few examples, Cohen and Rudolph³⁵ (1931) claim 83% cures and great improvements as the result of dietetic treatment, Stier and Hollister¹⁵⁷ (1937) obtained 78% from desensitisation, James¹⁰² (1933) 89% from argyrol tamponage, A. Francis⁶⁵ (1902) 86% from cautery, C. Francis⁷² (1934) 74% from cautery, Cooke and Grove³⁷ (1935) 82% from sinus surgery, Shields and Bailey⁸ (1937) 93% from zinc ionisation and in this series 74% from zinc ionisation.

What treatment, then, is the one to adopt when presented with a case of nasal allergy? This will depend upon the accuracy of diagnosis of the exact protein or proteins responsible. When one has the benefit of an allergist to make a series of skin tests /

tests, desensitisation or avoidance therapy, where possible, is the method of choice. In this country, however, skin testing is not so widely practised as in America, and the more general methods must be employed. These resolve themselves into surgery, cautery and zinc ionisation.

In Edinburgh we have not had the successes with cautery that Francis reported, although in many cases it provides a dramatic cure where other methods have failed. Sinus surgery in Edinburgh has failed so miserably to improve allergics that it is now condemned. The criticism that could be levelled at the Edinburgh surgical treatment is that it is not sufficiently radical. The American authorities are of the opinion that nothing but extreme radical surgery will be of any use. They perform double radical fronto-ethmoido-sphenoidectomies and double radical antrum operations. Such an operative procedure would never be tolerated by patients in this country. In addition, these extreme nasal operations are not performed under local anaesthesia here and asthmatic patients cannot stand the length of general anaesthesia necessary. In America local anaesthetic is the method of choice.

Another objection to the sinus surgery procedure is that in the cases which do not improve no further treatment can be instituted. There is too much tissue destruction for any further lines of nasal treatment /

treatment to be tried. I feel that one should first use the more simple measures which do not lead to so much interference with normal nasal physiology and anatomy. Such a line of treatment can be found in zinc ionisation or cautery. My preference is for the former therapeutic measure as the results are better in the hands of the majority of specialists. Few other people can equal Francis' figures with cauterisation. In addition, the percentage of cures by cautery following a failed zinc ionisation is higher than that obtained by ionisation after a failed cautery. In other words, zinc ionisation leaves the nose in a state in which other methods of treatment may be successfully employed.

I would suggest, then, that a case of nasal allergy, be it hay fever, vasomotor rhinitis or asthma, should be treated by zinc ionisation in the absence of frank sinus infection or true turbinate hypertrophy. If necessary, for convenience of packing, a submucous resection may first be performed, or polypi removed. By means of zinc ionisation some 80% will be cured or greatly improved. In those cases which do not respond, further treatment will depend upon the state of the nose. If the turbinates be still pale and oedematous, cautery should be applied to shrink them and to destroy any trigger areas. If the turbinates be actually hypertrophied with enlarged posterior ends, they /

they must be trimmed and the posterior ends removed. This regime, in conjunction with general therapeutic measures, avoidance therapy, etc., should produce something over 90% of cures and great improvements.

OTHER USES OF IONISATION.

I have treated a number of cases by zinc ionisation to see whether it is a panacea for all forms of rhinorrhoea. Four cases of persistent nasal catarrh following radical antrum operations have been treated with no benefit whatsoever. The discharge was still complained of, and the headaches were unaffected. These cases, of course, had no allergic basis and the conclusion one would draw is that ionisation is of no value at all in the presence of pus in the nose.

One interesting case of Besnier's prurigo (an allergic eczema) has been treated. She had no symptoms at all of nasal allergy, although her turbinates were slightly pale and swollen. After three treatments she was so much better that her name was removed from the Waiting List of the Skin Department of the Royal Infirmary.

Beck" (1939) has reported the successful use of ionisation in epistaxis. The results are due to the membrane formed by the ionisation and to the fibrosis produced round the blood vessels.

SUMMARY.

1. A review of the literature on nasal allergy has been made with special reference to zinc ionisation therapy.
2. Mention has been made of the methods of investigating a case of nasal allergy and the results of various forms of treatment are given.
3. The technique of zinc ionisation is described and the details requiring particular attention are mentioned.
4. Zinc ionisation acts by coagulating the surface epithelium with a subsequent regeneration of healthy epithelium, and by reducing oedema in the nose as a result of fibrosis in the submucosa.
5. Zinc ionisation may be used for any form of nasal allergy. The results of 120 cases treated personally are given in full. These show 30.92% cures, 42.73% great improvements, 15.45% improvements and 10.90% failures.
6. No untoward effects have been noted in a total of 492 ionisations.
7. The cases which have failed to respond to zinc ionisation are described and commented upon.
8. Zinc ionisation has no effect at all upon purulent nasal discharge.
9. An outline of the treatment to be adopted in any particular case of nasal allergy is given.

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