"PRESENT DAY VIEWS OF ASTHMA WITH SPECIAL REFERENCE TO ETIOLOGY AND TREATMENT AND INCLUDING AN ANALYSIS OF 117 CASES."

by

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CONTENTS.

INTRODUCTION.

Since I joined the Colonial Medical Service, British Guiana in September 1927 I have had the privilege of observing and treating a large number of cases of asthma at the following hospitals in the colony.

(a) Mental Hospital, Berbice for two years.

(b) Public Hospital, Bartica for three months.

(c) Public Hospital, Suddie for two years.

It is in the last named hospital most of my observations have been carried out.

The population of British Guiana consists mostly of East Indians and Africans and a few Europeans, Chinese and the "mixed" people.

Asthma is a comparatively common disease in British Guiana. The Surgeon General's Annual Reports for 1929 and 1930 show that during the year (1) 1929 at the Public Hospital Suddie 529 males and 380 females, a total of 909 cases of asthma were treated at the out-patient department and there were 100 cases of asthma treated as in-patients; during the year 1930 at the same hospital 785 males and 720 females, a total of 1,505 cases were treated at the out-patient department and there were 139 cases of asthma treated as in-patients. These figures do not give the incidence of the disease since one case may be treated several times during the year and so also one case may be admitted several times during the year. Nevertheless, asthma judging from these figures is undoubtedly one of the commonest respira-

tory diseases, occurring in this part of the colony. It is most common among the East Indians and the Africans who form the labouring class and the bulk of the hospital patients.

The result of this paper is over four years experience in studying the disease in the hospitals mentioned above and it is my intention to deal with the etiology and treatment of the disease in the hope that further light may be shed on this distressing and mysterious malady.

Summary of Literature & Historical Remarks

The older writers, as sometimes happens even today, had used the term asthma to indicate dyspnoea due to such conditions as intra-thoracic tumours, renal, cardiac, haemic and pancreatic disease as well as the broncho-spasm which is one of the manifestations of the syn-drome which clinicians today designate as asthma. Thus Hippocrates (2) (460 B.C.) and the physicians of the first and second centuries employed the term to indicate certain types and degrees of breathlessness. Celsus for example thought it was a difficulty in breathing intermediate between "dyspnoea" a relatively mild form (3) and "orthopnoea" the most aggravated state. He believed also that the "Sibilus Noise" produced during respiration in certain forms of dyspnoea was due to "constriction of the respiratory passage".

Again Aretaeus (120 A.D.) although giving a good description (4) of an asthmatic attack classified the breathlessness following running or laborious work under the head of"asthma" and included orthopnoea in the same category.

Caelius Aurelianus (fifth century A.D.) was the first (5) to give an accurate description of an asthmatic attack and observed the fact that the disease occurs in infancy and frequently follows after heavy colds.

It is to be noted further that most of these early writers thought that asthma, like certain

other obscure diseases, was caused by"humors,vapors, fluxions,or pituita" which irritate the lungs.

Van Helmont (1577 - 1644) was perhaps, the first to introduce the concept of a "nervous" or "spasmodic " asthma characterised in its occurrence in sudden attacks and in this respect simulating epilepsy.(6)

Thomas Willis (1621 -1675) emphasized the convulsive nature of asthma and noted that many emotional causes may precipitate an attack.(7)

Etmuller (1688) made a careful study of the disease in children and recommended vomiting for the relief of an attack, a practice which many physicians today still employ in the treatment of an attack in children.(8)

Floyer (1698) a sufferer of the disease, wrote a splendid treatise on the subject. He divided asthma into two types, one he called "continued" asthma caused by some definite organic pathology which is usually manifest, the other he termed "idiopathic " , "convulsive" or periodic flatulent asthma" since the cause was less obvious and suggested it was due to the "constriction of the bronchi and bladders of the lungs by windy spirits".(9)

He stated that he was told that his asthma started in his tender years and reflecting on the hereditary factor he wrote, "As my asthma was not hereditary from my ancestors, so, I thank God, neither of my two sons are inclined to it, who are now past the age in which it seized me".

Cullen[10] (1770 - 1800), the great authority of his time supported the theory of the nervous spasm and was inclined to the belief that it was hereditary.

Bree (1800), a martyr to the disease, believed that[11] the primary cause of asthma was an exudation in the bronchial tubes and that the paroxysmal attacks were an attempt on the part of the respiratory organs to get rid of an irritant either in the lungs or in some organ which those muscles serve. He divided asthma into four species based on etiological factors. Thus he stated that in one specie the "wheezing" and straitness are occasioned by the obstruction of lymph and by the state of the stomach and oesophagus which was a remote cause preceding the difficulty of breathing in a fit.

Bostock (1819) thought that some organic injury to the lung[12] was the essential cause.

Laennec (1835) the inventor of the stethoscope , divided[13] asthma into two varieties,"one ,asthma attended with puerile respiration in which the vital expansibility of the lungs is increased from a temporary augmentation of the respiratory necessities of the system occasioned by some unknown modification of the nervous influence; the other, spasmodic asthma, from a spasmodic contraction of the air tubes".

Ramadge (1847) also thought there were two types of asthma[14], one he termed the essential or nervous, the other he designated the complicated or spasmodic.

Salter (1860)[15] in his classic monograph pointed out

that in the asthmatic there is " a morbid proclivity of the musculo-nervous system of his bronchial tubes to be thrown into a state of activity, the stimulus may be either immediately or remotely applied but in either case would not normally be attended by any such result." He was the first to emphasize the association of animal emanations and the hereditary factor.

Leyden (1872) thought certain small octahedral crystals (16) seen in the sputum of asthmatics acted as irritants to the bronchial mucuous membrane.

Curschman (1882) observed spirals in the asthmatic sputum (17) and thought they were the cause of the attacks through an exudative process.

Meltzer (1910) Observed that there was a similarity of symptoms (18) and bronchial constriction in animals dying of anaphylactic shock and those of asthma and suggested that asthma was an anaphylactic phenomenon.

From this brief review of the literature it is observed that up to the early part of the nineteenth century the term asthma was applied to all types of disordered respiration and difficult breathing. Within the last generation, however, improved methods of diagnosis has led to a clear differentiation of the dyspnoea due to various organic diseases and that forming a part of the syndrome of symptoms which we now term asthma.

Further early workers failing to find a cause of the disease began to seek an explanation of the cause of the dyspnoea until there sprung up two

schools of thought - one believed that the dyspnoea was due to swelling of the bronchial mucuous membrane and the other that it was due to spasmodic contraction of the bronchial muscles. Most authorities today are inclined to the latter view but also admit that there is an associated turgescence of the bronchial membrane. Thus Mc Dowall (19) (1930) in an etiological survey of the subject states that "from the point of view of the physiologist the condition of asthma must be looked upon essentially as a symptom which indicates bronchial constriction and probably some turgescence".

During the present century intensive laboratory investigations have been combined with the older clinical methods and it has been shown that various factors probably enter in the production of the disease.

Reviewing the history of the treatment of the disease it is found that in early times, the etiology of the disease being obscure, the treatment was palliative and very varied. Smokes from various medicinal herbs and gums e.g. stramonium, belladonna, tobacco leaves opium etc. were inhaled and often gave some relief for a time. Cathartics, emetics, diaphoretics, bleeding, diuretics etc. were all given a trial with varying results. In some cases marvellous cures were claimed while in others the same drug made the patients worse.

Passing on to modern times, Solis- Cohen a sufferer of asthma in 1898 introduced adrenal substance[20] in 5 grain tablets orally two or three times a day, as a valuable means of treatment.

Takamine in 1901 produced from the gland the active principle[21] called adrenalin. This drug is administered subcutaneously and is the best remedy to relieve a paroxysmal attack of asthma.

Within recent years, ephedrine an alkaloid obtained from the Chinese herb, Ma Huang (Ephedra Vulgaris), has been given a fair trial.Its actions are similar to those of adrenalin. It has the advantage that it can be taken orally and its effects are prolonged for several hours, though the onset is not so prompt. It can be employed as a preventive and some who cannot take adrenalin can take ephedrine.

Adam (1900)[22] and Haseltine[23] are staunch supporters of the toxic factor and believe that asthma is a toxicosis or toxaemia arising partly in the nose and partly in the intestimes.

They advocate treatment of detoxication either by lessening absorption or by stimulating physiological elimination and attention to nasal abnormalties.

Recently asthma has been regarded by many observers as an allergic manifestation and these investigators treat the condition either by removing the patient from contact with the various exciting substances protein or otherwise, recog-

nised by dermal sensitisation test or by a process of dietetic error or by desensitising him to the substance or substances to which he is sensitive.

I think it will not be out of place if I end this summary of the literature with the following words of Hyde Salter(p.3) written in 1860 since they still apply today as they did then:- (15)

"Asthma is a disease about whose pathology more various and discrepant ideas prevail than about any other disease that could be named and to this day, if we appeal to the opinion of living authors, its absolute nature must be considered as still sub judice."

Like cancer it is a disease in which considerable progress has been made toward its elucidation and though it seems as if its conquest is not far off yet for no obvious reason it is unattainable. Cures have been recorded but statistics do not show that they are maintained without recurrence throughout the existence of the sufferer, and Hurst (p.7) has recently stated that he has seen numerous patients who,after thinking themselves (24) cured, have relapsed for periods varying between one and twenty five years.

There is evidence that different factors play their part in the production of this condition in individual sufferers. Thus in some, the disease is due largely to hereditary influence, in others it is allergic in origin, and still in others it is a

reflex phenomenon. Again some are toxic in origin while yet others appear to be purely nervous in origin. These various factors will be dealt with in more detail under the etiology of the disease. From a consideration of the various etiological factors it will be obvious that no fixed routine treatment can be adopted for each individual. A thorough investigation of each case is necessary to determine the best line of treatment to be adopted. With such an understanding of the disease the old-time pronouncement of physicians that, for asthma there is no cure, no longer holds good. Asthma is a condition the proper treatment of which demands patience in both physician and patient. Thorough investigation must be followed by thorough and sometimes long treatment and it is only by such means that success will be attained. Unfortunately often patients get tired of long treatment by their physician and go from doctor to doctor only to get a variety of treatment and in many such cases both time and money are wasted.

In conclusion there is evidence that quite a number of patients derive benefit under proper investigation and treatment and one hopes that with many diligent workers in the field the day is not far distant when every sufferer of this distressing malady will be able to secure relief and live an existence more like that of their normal fellow men.

PROCEDURE ADOPTED IN THIS REPORT.

In this paper 117 cases are reported. They were collected as follows:-

(a) 39 cases being the total number of asthmatic patients admitted to the Royal Infirmary Edinburgh in ward 28, during the years 1919 to January 1932.

(b) 23 cases from ward 22, the majority of which were treated as out-patients while a proportion of the more severe cases were treated in the wards for a time. By the kind permission of Professor D.M. Lyon they were all put at my disposal for investigation.

(c) 55 cases personally examined and followed up in British Guiana.

The ages of the patients ranged from one year to seventy four years. The patients are for the most part of the hospital class.

The cases collected from wards 22 and 28 were all recommended to hospital by their own doctor as cases of "asthma".

A diagnosis of asthma in all the cases in this report was based on a thorough examination of the individual and a careful history of the illness. Cases with obvious cardiac or renal disease were excluded. The cases personally investigated by the author in this report have been studied as follows. A careful history has been obtained in each case, the chief object being to discover the conditions and circumstances related to the attacks of asthma.

On account of the periodic or paroxysmal nature of the disease often the sufferer sought advice during the inter-paroxysmal period with the hope of preventing future recurrences. In an early case of asthma the only means of diagnosing the complaint in the inter-paroxysmal period is from the patients history, hence a thorough history is of the greatest importance in the investigation. The age and sex are noted. Then one enquires whether there is a hereditary taint in the family and elicits a brief history of the primary onset and associated conditions. Further, the nature of the symptoms, their season and manner of onset and whether they are periodic in occurrence, are investigated. Finally, following a thorough physical examination, relieving factors are noted.

The Family History is investigated to determine whether there is or has been (a) asthma;(b) hay fever ;(c) neurotic tendencies e.g.migraine, epilepsy, neuralgia, nervousness, insanity;(d) respiratory tendencies e.g. tuberculosis, bronchitis,frequent colds;(e) arthritic tendencies e.g. rheumatic fever, rheumatoid arthritis, rheumatism;(f) skin affections e.g. eczema, urticaria in near relatives - grand-parents, parents, uncles, aunts, brothers, sisters, sons, daughters, cousins and whether paternal or maternal.

A positive inheritance history makes the prognosis guarded since it has been shown that these cases

are less amenable to treatment. Further these cases are more likely to be frankly allergic in origin and will indicate the advisability of biochemical, bacteriological and sensitisation tests being performed .

The Age of Onset is noted since it helps in directing attention to the provocative factor of the attacks. Asthma occurring in infancy is practically always of the primary type and the allergen is usually found to be one of the common foods. Asthma starting in later life is more often due to hypersensitivity towards animal or vegetable emanations or to bacteria. Further, the earlier in life asthma starts the more likely are skin reactions to be positive and it has been shown that asthma arising the first five years of life and after middle life is less amenable to treatment. (25) The nature of the earliest attacks should be noted since if there is a history of recurrent colds or bronchitis leading eventually to outbreaks of asthma, a bacterial cause must be sought. On the other hand, if the attacks are ushered in by sneezing or profuse rhinorrhoea unassociated with any respiratory disease or preceded by urticaria or eczema allergism is suggested.

Sex. Asthma is said to be twice as common in boys as in girls, slightly more prevalent in females than males from the age of puberty to the menopause, after which it is slightly more frequent in males (p.241) (26)

Periodicity. The periodicity of the attacks should be noted especially in relation to the first few years of the disease.

Asthma frequently follows winter colds or the specific infections prevalent at those times and consequently in many instances immediately related to respiratory tract infection, whereas asthma occurring in summer is often due to hypersensitiveness to pollen or seasonal fruit.

The localities in which asthma is usually experienced or aggravated and those in which it never occurs or is ameliorated is investigated. Prolonged residence in cities may bring freedom from attacks of asthma, whilst a visit to the country may invariably result in a fresh outburst of symptoms. Occasionally the larger the city and the more centrally situated the patient, the less likely is he to suffer. Sensitiveness to trees or grass pollen is then suggested but in many of these cases no specific hypersensitiveness can be demonstrated.

On the other hand, some patients are always worse if living in a town, particularly in foggy weather. In such cases an underlying bronchitis or sinus infection should be suspected.

Asthma may occur in certain houses and never in others. These should suggest searching for a possible connection with objects such as cats, dogs, parrots, special bedding etc. which are recognised

as relatively common sources of allergens. If the attacks occur only at night one should investigate if there is any differences in meal times in the houses, or the composition of the bedroom dust. The nature of the patient's occupation should be investigated to determine whether there is any relationship between the two. Thus the baker may be intolerant to flour dust, the chemist to ipecacuanha and the groom to horse dandruff. The effect of odour and emanations should be thoroughly investigated as often the sufferer does not appreciate the ill effects of certain animal emanations.

Drugs One should always enquire whether the patient is in the habit of taking any drugs, since it has been shown that often a patient takes aspirin for an attack of cold or headache and is quite unaware of the possibility of his being sensitive to the drug.

Diet. Occasionally patients are sensitive to some article of diet but more often than not, the offending article is recognised and avoided. Often, however, patients give a positive skin reaction to different foods, exclusion of which, does not cure the asthma.

Finally, if no relationship can be detected between environmental conditions and the occurrence of asthma then a careful search should be made for localised infection e.g. septic teeth, sinus infection etc. or sources of reflex irrita-

tion such as constipation, intra-nasal deformities, wax in the ear, distended rectum or stomach and the like.

Physical Examination .

Besides the usual routine physical examination that is carried out in medical cases, special attention should be directed to the following points in the examination of asthmatics.

The nose, sinuses, throat, teeth, gall-bladder, appendix genito-urinary tract should be examined for signs of focal sepsis.

In the nose, one looks specially for the presence of infected sinuses, especially the eth-moidal air cells and the existence of oedematous polypi blocking the naso-pharynx, and which may set up reflex irritation.

If there is any suspicion of accessory sinuses infection, an X-ray examination should be made. The condition of the chest wall should be inspected to determine the degree of kyphosis and the extent to which this can be made to disappear on extension of the spine. The lungs should be examined for signs of permanent damage. Chronic bronchitis and emphysema are frequent complications and render the prognosis less favourable. It must be remembered, however, that the clinical signs of emphysema usually are more marked than the amount of actual damage which has taken place. The cardio-vascular system and renal function should be examined to exclude such conditions as renal or cardiac asthma.

It must be remembered also that aortic aneurysms, tumours of the mediastinum or of the lung, enlarged bronchial glands or enlarged persistent thymus may all give rise to dyspnoea.

The blood, urine, faeces and sputum should be investigated both during the spasm and in the interparoxysmal period, if possible.

The Blood. The Van den Bergh reaction, the differential count, the sugar variations and calcium content should be determined, if necessary. They should be performed on blood taken during or immediately after the asthmatic attack and again, if possible, in an interparoxysmal interval for the sake of comparison.

The Urine. Urinalysis should be done in every case if only to exclude a renal cause and in the primary cases, proteose estimation may be useful.

The Sputum. Typically this is not purulent and if so the diagnosis must be made with caution since there may be other underlying factors e.g. foreign body in the bronchus giving rise to dyspnoea. Infections of the entire respiratory tract may be responsible for repeated seizures either by reflex stimulation or by the production of hypersensitiveness to bacterial products and in such cases autogenous vaccine therapy gives quite encouraging results.

The Faeces. Again if the history indicates that there is some relationship between digestive disturbances, certain foods or constipation and the

attacks of asthma, then an examination of the faeces should be made for the presence of imperfectly digested foodstuff and abnormal bacteria.

Skin Tests. These should be performed when the history indicates it. The principle of these tests depends on the fact that if a specific allergen is introduced into the skin of a sensitive individual it will produce a reaction in the form of a raised red wheal which occasionally sends out branches like pseudopods in all directions. Further, the whole may be surrounded by an erythematous zone. The size of the wheal may be an inch or more in diameter and must be compared with that resulting from a control inoculation with the allergen solvent only.

Two methods of application are usually employed.

The Scratch Method. The anterior aspect of the forearm is cleansed with spirit and by means of a sharp scalpel or vaccinostyle small incisions about ¼ inch long are made about one and a half inches apart. Care is to be taken that the scratch is sufficiently deep but that no blood should be drawn. A little sodium hydroxide solution and a little of the test paste are applied and rubbed into the wound by means of a piece of match stick - a clean one being used for each test or by a glass rod which should be cleansed after each application. A control scratch into which deci-normal sodium hydroxide only is rubbed must always be made since some individuals react quite briskly to the slight trauma and solvent alone. When the reaction is positive, a surrounding

flush and itching are observed in about ten minutes and a well-formed wheal in ¼ hour. The history will indicate to some extent what allergens would be likely to give positive results and tests with these usually in groups, should be tried first. If any one group gives a positive reaction, then its individual components must be tested separately in order to incriminate the offending member.

The Intradermal Method. This gives far more positive results than the preceding method and consists in injecting a solution of the suspected substance or group of substances into the skin of the arm or fore-arm at points spaced about one and a half inches apart. 0.05 c.cm. of the solution to be tested is injected intradermally and again a control must be done. A few finely graduated syringes are required since a clean syringe is necessary for each test. The significance and ultimate therapeutic value of skin tests are still debatable points.

On the whole in this series the results of skin tests (the scratch method being employed) have been disappointing in that only 18 cases (25 per cent) out of 73 cases tested gave a positive result to one or more of the substances tested. Further positive results were only of value when compatible with the patient's history e,g. if the patient gave a positive reaction to eggs and milk and could take these with impunity during the intervals of the attacks, the test was more or less disregarded.

Of the 18 cases that gave a positive reaction in

only 5 cases (7 per cent of the number of cases tested) were the tests compatible with the patient's history.

CLINICAL FEATURES.

Asthma clinically could be divided into two types, one in which there is usually a family history of asthma, hay fever or other allergic manifestations such as eczema, urticaria, cyclic vomiting or migraine. This type is termed "primary" for convenience and usually begins in childhood. The other type, termed "secondary," usually follows some respiratory affection and may follow Measles, Whooping Cough, Bronchitis or Pneumonia and usually begins in later life.

Asthma is a condition characterised by attacks of severe dyspnoea recurring periodically. The patient is often wakened with a sense of suffocation and air hunger. If the attacks come on when he is awake there may be prodromal symptoms or an aura such as itching of the nose or chin, sneezing, coryza, restlessness, polyuria, loss of appetite, mental exaltation sometimes depression or oppression in the chest.

In this series one or more of these prodromata were present in 74 cases (63 per cent). The aura is soon followed by a feeling of oppression in the chest and soon after by the marked dyspnoea. During the attack the chest is filled in the position of full inspiration, expirations are loud and prolonged, the great difficulty throughout being to empty the chest. The patient is usually pale with an anxious expression and profuse perspiration pouring out all over his body.

In severe attacks there is usually cyanosis and the patient usually sits up in bed and fixes the shoulder girdle by grasping ahold of the sides of the bed. By this means he brings into play his extraordinary muscles of respiration. In this position, he seems to be trying to squeeze air out of his chest. All the extraordinary muscles of respiration are brought into action and the vessels in the neck in severe cases become engorged. The respirations are not increased in rate and the pulse is small and usually slightly quickened. It is often 85 to 115 per minute. The blood pressure usually falls. Ultimately when the distress is at its height, the paroxysm diminishes and the attack ends, leaving the patient exhausted but apparently none the worse of the attack. The duration of an attack varies from a few minutes to several days. It usually terminates gradually, sometimes rapidly. At the end of the attack usually, the patient coughs up pellets of viscid sputum which is never purulent unless there is some other associated condition.

It may contain Curshmann's spirals, Charcot Leyden Crystals eosinophiles and various bacteria. Curshmann's spirals appear in the sputum like grains of sago. They can be unravelled if placed in water and are then shown to consist of fine mucous spirals about one inch long which are wound round a central core.

They are supposed to be allied to small bronchial casts. Charcot Leyden Crystals are colourless, pointed and octahedral in shape and consist largely of phosphates in combination with an albuminous body.

The blood. This usually shows an excess of eosinophile cells. Recently Dr. Marjorie Gillespie (27) has stated "that of the cases she has studied in six months (total number not stated) only two had eosinophile count of less than 4 per cent, while the normal count is usually 2 per cent. The average count in these patients was somewhere between 7 & 10 per cent. The eosinophilia varied according to the state of the patient. During an attack in the majority of cases there was a fall to perhaps half the former percentage". On the contrary other investigators report a rise in the percentage during an attack. Thus Claude determined the percentage of eosinophiles (28) every ten minutes during an experimentally produced attack of asthma and found 8.3, 6.4 and 5 per cent. The same patient before the attack had 5 to 6 eosinophiles per cent. Again Bezançon and de Jong (29) state that "all the researches establish that there exisits during the asthmatic paroxysm a marked blood eosinophilia of 6 to 12 per cent or sometimes more and that between the attacks the count is most often normal or sometimes slightly raised."

Physical Signs (during the attack)

Inspection.

The expression is one of anxiety. The eyelids may gape and the eyes become prominent. The pupils are usually dilated and there may be cyanosis in severe attacks. The patient may be unable to speak above a whisper apparently because there is not enough air expired to allow of true phonation. The chest is fixed in the position of full inspiration, it is therefore distended and moves very little with breathing. Loud wheezing is usually heard with expiration. The chest appears barrel-shaped as in emphysema.

Palpation. This reveals absence of movement and the presence of rhonchial fremitus.

Percussion. This shows the note over the whole chest to be hyper-resonant.

Auscultation. The breath sounds are harsh vesicular in character, inspiration being very short, expiration loud and prolonged.
Rhonchi of all pitches are usually present all over the chest. The vocal resonance is not altered.

Physical Signs (during the intervals of the attack.) There are no physical signs except those of emphysema or bronchitis should these be associated.

Organic Changes.

Chronic asthmatics usually present a peculiar physique and gait, in fact so much so that in many cases a diagnosis of asthma can almost be made by the appearance alone. The patient is usually thin, with elevated shoulders and frequently rounded back. The face bears a peculiar haggard and anxious expression, the eyes may be widely opened, slightly prominent and even blood-shot and watery. The patient walks in a peculiar manner, the body is held rigid, the shoulders are elevated and the arms sway to and fro pendulum-like.

The thorax is usually deformed owing to associated emphysema, the antero-posterior diameter being increased. Deformity of the thorax is common when the asthma starts in childhood and commoner yet if there is associated rickets. The various deformities met with are (a) depression of the sternum with indrawing of the cartilages of the lower fixed ribs.(b) "pigeon chest" or a prominence of the sternum with depression of the adjacent ribs.The muscles of the thoracic wall and some of those which pass from the chest to the spine or head e.g. trapezius and the sterno-mastoid tend to assume a new postural length and tone, perpetuating as it were, their abnormal state which is observed during an asthmatic attack. The result of this altered length and tone of the muscles

is that the shoulders become raised, the trunk becomes immobile and the thorax tends to be fixed in the position of inspiration during the inter-paroxysmal intervals.

The lungs at first show no organic change but from repeated attacks they become chronically distended and clinical signs of emphysema ultimately make their appearance. It must be noted, however, that the degree of true emphysema usually found after death in asthmatics is far less than one might think from the physical signs exhibited during life. The importance of this fact is that much can be done to restore the lungs to their normal condition whereas true emphysema is incapable of cure.

Cardio-vascular changes as a direct result of repeated paroxysms are rare but after emphysema and chronic bronchitis there is chronic venous congestion and ultimate failure of the heart.

Differential Diagnosis.

Asthma has to be differentiated from the dyspnoea of cardiac or renal disease, tumours of the lung, foreign body in the respiratory tract, the recurrent bronchitis of children and the severe bronchitis of old age. The differentiation is not difficult if the patient be studied between paroxysms. In all of these conditions the difficulty is with both inspiration and expiration and in none is the dyspnoea of the prolonged, difficult expiratory wheezing character, associated with bronchial asthma. Perhaps the so-called bronchitic asthma occurring in middle-aged persons may occasion some difficulty but the fact that it arises after a more or less lengthy period of bronchitic attacks, is ushered in by an outbreak of bronchitis and the presence of signs of bronchitis many weeks after the paroxysm, absence of family history or past history of associated allergy will all clench the diagnosis. Roentgen-ray examination of the chest may reveal signs of emphysema and of bronchial infection. Further, in chronic bronchitis the sputum usually is profuse and its production precedes an attack and likewise is coughed up during one. It is discoloured, yellow or green, purulent and contains no spirals or eosinophiles, but is loaded with neutrophiles and bacteria. There is no eosinophilia and a moderate leucocytosis is common. Skin reactions to allergens

are rarely obtained. Frequently in children the (30) catarrhal element obscures any evidence of spasm and the early attacks of asthma in childhood are generally labelled"recurrent or chronic bronchitis" until finally a typical spasm occurs. Repeated attacks of bronchitis in a child, especially in the presence of an allergic family history or evidences of other allergy such as eczema, nettle-rash, food upsets, or cyclic vomiting should always suggest an asthmatic diathesis.

Cardiac Dyspnoea is usually easily distinguished. The dyspnoea is associated more with muscular effort, of an accelerated inspiratory gasping or panting nature and aggravated by recumbency. Bloody froth which is usually tenacious with a tendency to stick to the mouth is usually coughed up. Further, the blood pressure is raised and there is more difficulty with inspiration whereas in asthmatics the blood pressure is relatively low and usually evidence of heart disease is absent.

There is almost always other signs of cardiac disease.

Renal Dyspnoea is comparatively rare and is usually a pre-uraemic condition occurring at a late stage in chronic interstitial nephritis when there are obvious signs of renal inefficiency such as raised blood pressure, hypertrophied heart, arterio- sclerosis, albuminuria and retinal changes.

Other Conditions. In children, other conditions giving rise to dyspnoea have to be excluded. The most important of these are a persistent and enlarged thymus, congenital laryngeal stridor, laryn-

gismus stridulus, and retro-pharyngeal abscess. A careful history and physical examination will be sufficient to avoid error.

In adults, the following conditions have to be borne in mind, tachypnoea of hysterical subjects and the difficult breathing associated with chronic pulmonary tuberculosis, pulmonary new growths and pathological states of the pleura, aneurysm, foreign body in the lung and the low type of pneumonia in advanced age.

In the tropics, helminthic infection, especially Ascaris lumbricoides should be excluded. The author has seen many cases of periodic dyspnoeic attacks due entirely to Ascaris lumbricoides infestation. Apparently the attacks of dyspnoea occur as a result of reflex irritation or whenever the worms have accumulated in large numbers in the alimentary tract. Often the diagnosis is only made when during the attack one or more of these Ascaris worms are vomited and helminthic treatment completely banishes further attacks. It is to be noted that in these cases too, there will be marked blood eosinophilia which may help to mislead the inexperienced. For these reasons, stool examination of cases in the tropics should be practised as a routine whenever possible.

Prognosis.

Death in an attack of asthma, although not an impossibility, is a most unusual event. Most of the instances reported have been in cases of long standing in whom the patient's resistance had been undermined by chronic bronchitis, emphysema and intercurrent debilitating illnesses.

As far as longevity is concerned, many asthmatics live to a good old age.

The age of onset is an important factor in prognosis. Thus if asthma starts in childhood there is great hope for spontaneous recovery to occur at puberty. On the other hand, if the condition starts in infancy and persists into adult life, organic changes will be more in evidence at middle age than if it started in the adult. Further, asthma appearing for the first time at middle age will in most cases persist throughout the remainder of the patient's life. In women, if the disease makes its appearance at puberty or the attacks recur regularly at the menstrual period, often recovery occurs at menopause. Usually asthmatics are less prone to diseases such as gastric and duodenal ulcers, diabetes and in children acute rheumatic fever (p.214)

If the attacks (26) are of long duration and the disease of long standing then the prognosis is worse. The frequency of attacks and completeness of recovery between them will also influence prognosis. Thus if the paroxysms are becoming more severe and more frequent as age advances and the unfortunate sufferer is

seldom free day or night from the distressing symptoms of his disease then the prognosis is distinctly bad since the loss of strength and appetite consequent to disturbed sleep and perpetual dyspnoea will certainly accelerate the advent of the final breakdown. If there is obvious organic disease of the lungs e.g. emphysema or chronic bronchitis and cardiac failure then the prognosis is less favourable. One must remember, however, that these complications may be more apparent than real and in that case more amenable to treatment. Chronic bronchitis is distinctly unfavourable for it tends to excite the asthma, produce emphysema, and put strain on the right side of the heart. The earlier the case is seen the better is the prognosis since greater care is taken to eradicate the disease before any permanent damage is done. Thus Lyon and Murray Lyon in a review of the results of treatment, state that "the duration of the disease before effective treatment is undertaken is of the greatest importance; the longer the delay the less satisfactory the result, although certain cases of long standing have benefited considerably under adequate treatment." (25) Unsuccessful previous nasal surgery complicates the prognosis and in many cases patients state that they are distinctly worse.

The prognosis is more favourable if some definite hypersensitivity is detected but even when the reaction agrees well with the history and other

features of the case one cannot be sure of obtaining good results in every instance. Patients who give small reactions do better than those who give very large definite reactions and those who react to several substances are more difficult to treat. Again, those who manifest no specific sensitisation are in a worse position but still here much help can be afforded these patients, although there is often no clear indication what to do. It may mean trying one thing after another. Vaccines, peptone and tuberculin therapy are all worth trying and often if one fails, another may succeed.

ETIOLOGY.

From very early times many theories with regard to the etiology of asthma have been propounded and as research has progressed, some have been rejected whilst additional evidence has been brought forward in support of others. During the last twelve years, every effort in research has been made to determine the fundamental cause of this distressing malady but unfortunately not even the most fanatically enthusiastic allergist would maintain that we have solved the problem of this mysterious disease.

I do not intend reviewing the voluminous literature on this part of the subject but I shall briefly review recent trends in the concept of the disease.

Before proceeding further, however, it must be stated that most authorities are agreed that no one theory will explain satisfactorily the diverse phenomena one encounters in this malady. There are probably elements of truth in most of them. Only time and experience can determine the relative merits of each.

In 1902, Richet and Portier (31) observed that on the second injection of a foreign protein into the blood stream of an animal after an interval of 9 - 14 days, the animal died of shock instead of developing an expected immunity. This increased susceptibility Richet termed anaphylaxis to express its antithesis to prophylaxis. During the first decade of the present century anaphylactic

experiments were being carried out by many workers and Meltzer in 1910 observing the similarity existing between the lungs of asthmatics and those (18) of guinea pigs dead of anaphylaxis suggested that asthma was an anaphylactic phenomenon. For years after, asthma was regarded as anaphylaxis occurring in man. Recently it was observed that paroxysms of asthma were especially common in persons who were subject to hay fever, urticaria, eczema and the various other symptoms associated with allergy. Gradually it became evident that the so-called "anaphylaxis" in man violated many of the principles of anaphylaxis in laboratory animals and finally asthma is now regarded by many authorities as an allergic manifestation.

The main differences between allergy and anaphylaxis as given by Coca, Walzer and Thommen in their book, "Asthma and Hay Fever in Theory and (32) Practice" (p. 131) are as follows.

(1) "the anaphylactic antibody which is common to all animals in which anaphylaxis occurs bears no relationship to asthma and the other common forms of human (atopic, allergic) hypersensitiveness such as hay fever, eczema, urticaria, food sensitivity etc; and that reagins, the antibodies most frequently associated with the latter group of hypersensitiveness, cannot be demonstrated in anaphylactic animals.

(2) the forms of hypersensitiveness which are responsible for asthma cannot be induced at will in the normal human being by any known method of

sensitisation nor can they be totally removed by any available methods of desensitisation, while both of these procedures may be regularly accomplished without difficulty in animal anaphylaxis.
(3) Asthma and some of the other expressions of atopic hypersensitiveness have been shown to be subject to an hereditary influence, which plays no part in anaphylactic sensitivity in animals.
(4) Most of the major immediate anaphylactic phenomena in animals have been found to be caused by a specific antigen-antibody reaction, which takes place in the smooth muscles of the shock organs, as well as in most other smooth muscles throughout the body and induces a violent spasmodic contraction of these muscles. On the other hand, most of the major immediate atopic phenomena in humans result from specific antigen- antibody reactions, which do not take place in the smooth muscles anywhere in the body. The result of such a reaction in humans, is almost always oedema and not muscular contraction. As oedema of the bronchial mucous membranes can explain the dyspnoea of asthma and the associated emphysema there seems no reason for discarding it as a satisfactory explanation of the asthmatic syndrome in favour of a phenomenon observed in the laboratory animal, the existence of which in man is doubted for the above mentioned reasons!

Although the immunological theory of asthma has

cast considerable light upon the nature and mechanism of the disease from a new and entirely different point of view, we are not justified, however, in assuming that all cases of asthma are allergic in origin, since our clinical observations prove over and again that many cases of asthma cured simply by the removal of polypi from the nose can be reflex in origin. See cases No. 2, 7, 15,21.

The allergists admit also that other factors play their part in the production of altered reactivity and that neither alone can produce the phenomenon. Thus Bray (p. 17) discussing the various factors in regard to the etiology of hypersensitiveness states (26) that it is by a blending of each that the most satisfactory viewpoint is obtained. Recently Hurst in a paper on the pathogenesis and treatment of (24) asthma states that he believes that "the asthmatic diathesis, the congenital and often inherited constitutional abnormality which is the one essential factor in the pathogenesis of asthma is caused by a slight deviation from the average blood chemistry which results in the vagal constituent of the bronchial nervous system being the predominant partner. In such individuals certain chemical, reflex and psychical stimuli which have no effect on normal individuals, gives rise to spasm of the bronchial muscles and hypersecretion of the bronchial mucous glands together with congestion of the bronchi, which is the natural accom-

paniment of their excessive functional activity. Hereditary and biochemical changes in the blood then, according to this authority, are the two factors which are most important in the etiology of the disease.

THE HEREDITARY FACTOR.

There is no doubt that in man a large percentage of cases of asthma show a definite familial taint while in others no such trait can be determined and it is admitted that in those cases the asthmatic diathesis or predisposition is acquired. Cooke and Vander Veer in a complete study of 504 cases found that there was a positive hereditary history of hypersensitiveness in 244 (48.4 per cent) (33) They found also that of 76 normal persons 11 (11.5 per cent) gave a positive antecedent (direct or collateral) hereditary history. From the marked contrast between these two figures they concluded that inheritance is a definite factor in human sensitization. Spain and Cooke in a study of 462 cases of asthma and Hay fever found that 270 cases (58.4 per cent) (34) showed a positive hereditary history. On examining 115 normal individuals representing 115 families they found 8 (7 per cent) with a positive family history. They concluded also from the striking difference in this percentage that in asthma and hay fever there is a definite inheritance factor. Balyeat in a study of 1000 cases of asthma and hay fever patients found that 60.1 per cent of all (35) cases studied gave a positive antecedent history.

Studying the history of 403 normal university students who did not have asthma or hay fever he found that only 9 per cent of their parents had asthma or hay fever. Thus he confirmed the findings of the above observers.

Bray in the examination of 200 children found that (36) 68.5 per cent gave a positive hereditary history. In the author's series 61 cases (52.1 per cent) gave a positive hereditary history for asthma or hay fever. Table I shows the findings of several authors who have investigated a large series of cases. The average of these reports on positive family histories is about 50 per cent.

TABLE I.

THE FINDINGS OF SEVERAL AUTHOR WITH REGARD TO A POSITIVE HEREDITARY HISTORY.

Authors	Number of cases	Percentage with positive Hereditary History
Cooke and Van der Veer	504	48.4
Spain and Cooke	462	58.4
Klewitz	423	35.0
Coke	1000	52.0
Peskin	278	42.5
Rackeman	1074	42.0
Lyon and Murray-Lyon	291	41.0
Sang	117	52.1
Rowe	234	56.4
Bray	200	68.5
10	4963	496.3
		49.63

The inheritance can be transmitted from parent to offspring in one of two ways either through the germ plasm or through the placenta. Most of the pre-ponents of the hereditary nature of asthma believe that the disease itself is not inherited but the underlying tendency, of which asthma is an expression and is transmitted through the germ plasm. Clarke, Donnally and Coca have shown that in cases (37) of pure uncomplicated asthma, there is among the progeny a greater incidence of asthma than of any other form of atopy or allergy pointing to a predisposition of the shock organ as well as a general hereditary tendency to atopy. It is doubtful, however, whether such a shock organ is inherited in man. It is generally agreed that an apparently normal individual whose antecedents and whose brothers and sisters are sensitised frequently does transmit something to the offspring, but of what this factor consists it is diffult to say.

THE BIOCHEMICAL FACTOR.

Recently much research work has been and is still being carried out along these lines and great hope is entertained that this sphere is the most likely to solve the problem. It is a recognised physiological fact that slight changes in the blood chemistry of man or animal can lead to profound metabolic changes and consequent pathological results. Oriel (38) and Knott (39) have shown that asthma cases tend to fall in two groups namely, one in which asthma is associated with allied diseases

such as migraine, biliousness in childhood, eczema, urticarial skin rashes, hay fever, and the other in which the only complaint is asthma itself. In the first group there was excess of amino-acid and bile pigment in the blood, the urine showed chemical abnormalities and there was decomposing protein material and putrefactive bacteria found in the intestines. In the second group there was little or no intestinal derangement detected. Cases are usually secondary to respiratory infection and occurred more commonly in later life. Further, Oriel (40) has shown that in the urine of asthmatics and other allergic conditions there occurs an ether-extractable nitrogenous substance which he terms a "proteose". This substance is found in small amounts in normal urines but in allergic conditions Oriel claims that the urine contains much more of this proteose which may then account for 1 to 5 per cent of the total urinary nitrogen. There is increased excretion of proteose during the activity of the disease and it may disappear during the periods of remission. Further Oriel and Barber (1930) (41) state that each patient gives a positive skin reaction when injected intradermically with his own proteose or with that from a similar case (but not with any other) and that after a graduated series of injections of his own proteose the patient may show definite clinical improvement. Murray-Lyon, Percival and Stewart (42) in Edinburgh and Freeman (43) in London have been unable to confirm the specificity of this

substance. Further research and trial are necessary before any definite pronouncement as to the significance and ther-apeutic value of this substance can be made.

Again Bray (p.157) has found that in untreated asthmatic children, the plasma bicarbonate content is toward the high limit of normal and is generally higher than that of their normal unaffected brothers and sisters. During attacks, this value falls from the alkaline toward the acid side. The normal limits in children for the plasma bicarbonate is from 0.022 to 0.028 molar, the drop occurs from the latter to the former.

Formerly, it was also claimed that in asthmatics there was a low blood calcium content. Thus Billigheimer found that in asthma the blood calcium is reduced and Novak and Hollander (1923) found a constant low serum calcium in some cases of hay fever and asthma. Several other observers, on the other hand, have found a normal amount of blood calcium in asthma. Thus Sonnenschein and Pearlman (1924) showed that there was a normal blood calcium in asthma. Bray and Payne (p.161) also have always found a normal blood calcium content in allergic children. Cohen and Rudolph (1930) in a series of ten patients with urticaria, vasomotor rhinitis and asthma, gave each, over a period of a month, at least 8 ounces of Calcium Sandoz by mouth and from 120 to 150 c.c of calcium sandoz intravenously or intramuscularly. In not a single

instance was there any amelioration of the symptoms and so they concluded that calcium therapy was of little or no clinical value in allergy. It is known that stimulation of the vegetative nervous system is associated with changes in the concentration of certain ions (p.53). The existing evidence, however, is not sufficient to establish whether (48) ionic concentrations are the cause or the effect of stimulation of the vegetative nervous system. Again residence at a height of over 4,000 feet cures the asthmatic and why this altitude should have this remarkable effect is still a debatable point. Storm van Leeuwen attributes the effect to the absence of allergens and other irritants in the air of high altitudes. Hurst, however, surmises that it will be found that the lowered oxygen tension leads to (24) biochemical changes in the blood, which result in diminution in the irritability of the bronchial nervous system.

Bray in an analysis of 200 asthmatics aged from 6 months to 12 years found that 4 out of every 5 (49) asthmatic children, the response of acid gastric secretion was below the average normal. Hurst believes it is due to chronic gastritis since normal secretion may be restored by repeated gastric lavage over long periods. Bray (p.167) suggests that this is one of the methods by which foreign protein gains (24) easy access to the body and that the substances which produce the reaction, are not destroyed in the digestive processes. "The products of protein breakdown do not produce allergic reactions", he states.

Further, he finds that with acid therapy there is an immediate improvement in appetite, an increase in weight and much sounder sleep. The attacks become progressively shorter in duration, less in intensity, diminished in frequency and after some 3 to 4 months cease.

The significance of these various changes observed is still debatable. Dresel and Katy (quoted by E. Billigheimer,Klin. Wchnschr. 1922,1,1601) put forward the theory that nerve stimulation results from ionic concentrations in the tissues and Zondek (quoted by E.Billigheimer,Klin. Wchnschr. 1923,2, 1082) has also pointed out that potassium and sodium ions stimulate the vagus whereas calcium ions depress it. These observations and similar work of physico-chemical nature which is engaging so much attention at this time indicate how involved these processes become and considerable research is still necessary to lead to a clearer understanding of these various findings. McDowall in a recent etiological survey of the disease (19) states that apparently what Hurst has described as a hypersensitiveness vagus centre is really a hypersensitive vagus nerve. Further, he points out the significant fact"that introduction of some forms of protein into some animals (but not all) causes a greatly increased sensitivity of the vagus. He states that if peptone made from foreign protein is injected into the blood stream the slowing of the heart and constriction of the bronchi caused by pilocarpine -- the drug by which vagus stimulation can most conveniently

iently be brought about -- is enormously enhanced and a dose which normally would have little effect may almost kill the animal". Stoland, Sherwood and Woodbury (1928) also found that excitability of the vagus is increased by the previous injection of (50) foreign sera and Freundo and Gottlieh (1922) have shown that peptone of foreign serum causes an enormus increase in the salivary response to pilocarpine. What varieties of foreign proteins could produce hyperexcitability of the vagus nerve have not yet been determined. From these observations and the fact that Prausnitz-Kustner reaction (19) indicates that foreign protein can easily get into the blood, it may be that in asthmatics some abnormal proteins, probably of a histamine nature, enter the blood stream and render the vagus hypersensitive. Further Pickering has shown that in certain conditions of the alimentary tract (53) imperfectly digested protein may enter the blood, probably in the form of peptone and initiate an attack. Sutherland also points out, that histamine, a break down product of (54) protein, can produce all the phenomena of pure asthma and recent research has shown that certain bacteria living in the bowel and respiratory tract are capable of producing histamine-like substances. Thus Koessler and Hanke (1922) found that the human colon contained a large amount of histamine and together with Shepherd (1928) they showed that histamine could be produced by many members of the coli-typhoid group. Further Koessler found that histamine formed in the bowel is rendered inert in its passage

through

through the intestinal wall. This has been shown by Best and McHenery (1930) to be due to the presence of a histamine inactivating substance which on (57) account of its enzyme nature they have named histaminase. This enzyme in the dog is most abundant in the kidneys and intestines. From these observations then, it is possible that if for some reason or other, there is deficiency in amount or activity of this histaminase in the bowel, an excess of histamine-like substances may enter the blood stream and cause asthma. Again Knott and Oriel have detected histamine-like substances in asthmatics and (58) other sputa. These they believe, are derived from gram negative bacilli allied to B.Friedlander group since culture extracts of these bacteria produce similar effects to those from the sputum itself and they suggest that the growth of these bacteria within the bronchial tubes and consequent production of these histamine-like substances, form one cause of locally produced asthma. Further, Thornton in 1930 using the preparation of the isolated bronchi, as (59) prepared by McDowall, has shown that histamine acts in constricting the bronchi when applied locally. In view of the fact that supra-renal dysfunction is suspected by many as the cause of the attacks, it is interesting to note that Dale has shown that histamine stimulates the production of adrenalin which (60) neutralises its action. From the foregoing observations, it is suggested that in many cases of asthma, there is an excessive production of histamine-like substances by bacteria, in some cases in the bowel,

and

and in other cases in the respiratory tract, and an inability on the part of the body to deal with this poison, and in view of Dale's observations there is probably also exhaustion of supra-renal secretion consequent on circulation in the blood stream of an excess of histamine-like substances produced by bacteria as stated above.

To sum up the foregoing observations, it is seen that asthma is a symptom complex which may depend on several different mechanisms. Hurst believes that in asthmatics there is a hypersensitive vagus centre while McDowall postulates a hypersensitive vagus nerve.

Biochemical changes in the blood and urine have been observed but the existing evidence is not sufficient to establish whether they are the cause or the effect of stimulation of the vegetative nervous system. From the foregoing remarks on the hereditary factor, the asthmatic then is an individual with usually an hereditary, sometimes acquired tendency towards a particular pathological process which in turn is intimately associated with a hypersensitiveness to particular foreign substances. On adequate contact with these substances, asthma results. The asthmatic paroxysm, however, is dependent on vagus stimulation. From the evidence brought forward, it is suggested that in many cases foreign substances probably enter the system of the asthmatic either through the respiratory tract or through the alimentary tract and lead to asthma but how they stimulate the vagus

nerve

nerve endings is unknown.

TOXIC FACTOR.

Since 1900 Adam claimed that asthma with all its vagaries is primarily a toxic condition. He bases his statement on the following observations :- (22)

1. Week-end periodicity is common and occurs in about 60 per cent of cases. In the author's series the occurrence of week-end periodicity is much less and is about 20 per cent.

2. The strenuous life and not too generous feeding of the army cured many men who found asthma recur on their return to the softer conditions of civilized life -- who again became well by attention to diet and open air exercise.

3. 50 per cent of cases start before puberty at a time when infections and exanthemata are most rife. 25 per cent of these children have skin affections, mostly characterised by itching. These affections correspond to catarrhal and spasmodic manifestations in lungs and larynx and Adam regards them as due to a general toxic state.

4. Sallow skin and cachectic appearances are common in chronic asthmatics and this indicates a toxic state, probably connected with adrenal defect and often disappearing together with improvement of the asthma after effective detoxication.

5. By attention to diet and hygiene and a weekly blue pill the symptoms are relieved. Cameron also supports the toxic factor in asthma and believes (61) the chief source of the toxicocis was the bowel with consequent impairment of liver efficiency.

Eustis found in 121 cases of spasmodic bronchial asthma intestinal toxaemia as determined by the (62) presence of putrefactive products in the stools. He suggests that toxic amines formed by intestinal putrefaction are split up by the normal individual and that asthmatics have lost this power. Haseltine about the same time as, and quite independently of Adam found that toxaemia and nasal irritation (23) are the essential factors in asthma. In 1929 he stated"that all patients showing symptoms of bronchial asthma are of an abnormal condition of the kind generally designated as a toxicosis or a toxic state". (23)

Toxaemia is the fons et origo of many illnesses of mankind and that bronchial asthma is in many cases due to toxaemia is well illustrated by the following cases :-

CASE 4.

Girl aged 12 years. School-girl.

HISTORY.

Asthma started at age of 5 years, after an attack of measles. Attacks occur at irregular intervals and usually at nights about 2 hours after going to be. Had treatment from several doctors but with no relief. Had urticaria for the last year off and on. Acne Vulgaris on face for about 2 years. Bowels move every other day but considered not constipated by patient. Hereditary history -- maternal grand-mother asthmatic. Skin tests negative.

On examination patient is anaemic, and poorly developed. No physical signs in chest and nothing abnormal

mal in ear, nose, and throat.

TREATMENT.

Calomel grains 3 and magnesium sulphate was given and she was instructed to attend lavatory at the same hour daily whether there was the desire or not, in the hope that a habit might be formed and bowels may act daily instead of every other day. She was also given a diuretic mixture consisting of pot. citrate grains XV, Spt. Ether. Nitros. minims XXX, Liq. Ammon. Acet. one drachm, Syrup Tolu one drachm, aq. ad ½ ounce, 4 hourly, and told to eat fruits regularly and take water freely.
This treatment was given in the belief that in this case there were toxic products being absorbed some where in the body and elimination by this means will bring some relief if not cure. The result was very encouraging. After a fortnight's treatment urticaria and acne disappeared and six months after patient reported well and stated that there were no further attacks of asthma.

CASE 8.

Male aged 24. Occupation Clerk.

HISTORY.

Complains of itching and redness of the skin (urticaria) of sudden onset. He consulted his doctor who made a thorough physical examination and gave him a bottle of medicine and told him to remain at home and take nothing but milk for a few days and then add fish, vegetables, chicken and meat daily in that order so that if there was an offending article in the diet it would be "spotted"

and

and could then be eliminated. He was of the opinion that such was the case here. After a week's treatment there was no improvement and no offending food was detected so his doctor began giving him adrenalin injections twice weekly and calcium lactate orally but all to no avail. After some weeks he was inclined to be short of breath, often felt tightness in the chest, while sitting quietly at home, and his itching was just as bad, if not worse than before, so he came to hospital.

On examination there was urticarial rash about the chest, abdomen and arms and auscultation of the chest revealed rhonchi of all pitches and vesicular respiration with prolonged expiration throughout the chest -- asthma. His maternal uncle and aunt both suffered from asthma. Blood examination showed a 10 per cent eosinophilia. Skin tests were negative.

He was put on the same treatment as case No.4 and in 10 days all signs of urticaria and asthma disappeared. For two years I have been able to keep in touch with the patient and there has been no recurrence of urticaria or asthma.

COMMENT.

The interesting points about this case are there was prodromal symptoms of tightness in the chest and tendency to be short of breath without exertion. Although a paroxysmal attack did not occur, yet there were physical signs of asthma present in the chest and a marked blood eosinophilia. There was a positive hereditary history. The

importance

importance of early treatment is well illustrated -- no return of symptoms for at least two years and cure in 10 days.

CASE 12.

Female aged 20. Housewife.

HISTORY.

Has had asthma since the age of 14 years. Begun after an attack of pneumonia. Attacks recur at irregular intervals sometimes free of attacks for months. Always has a "chronic cold in the head". Had treatment from many doctors for asthma but got no relief. Brother asthmatic in childhood but cured on attaining puberty. On examination of the nose pus was seen coming from her left middle meatus and drainage of the left maxillary antrum resulted in a complete cure of her asthma. Cases of this kind are common in the experience of the author and tempts one to conclude that toxaemia alone can lead to the asthmatic state and associated bronchospasm.

THE NASAL FACTOR.

Herck of Freiburg in 1844 was the first to recognise (63) the importance of the nasal factor. Subsequently many observers published cases as having been cured by removal of polypi or attention to some other nasal condition. Thus Voltolini in 1872 reported (64) eleven cases of asthma cured by removal of nasal polypi and Frankel in 1874 showed that asthma was associated (65) with chronic nasal catarrh as well as with polypi. Adam of Glasgow and Haseltine in America (22) for the last 30 years (23) have advocated that asthma is due to toxaemia the most common source of

which

which is chronic nasal infection. Dixon and Brodie in 1903 finally proved experimentally that stimulation of the mucous membrane of the nasal septum in its upper and posterior part can reflexly produce bronchial constriction. (66) Ever since many physicians look to the nose as the chief factor in the causation of bronchial asthma. The results of treatment and the fact that not all nasal polypi, infection and other causes of nasal irritation are associated with asthma, do not lend support to such a theory. Undoubtedly, however, there are cases of asthma whose symptoms are due to indirect reflex stimulation of the vagal centre since removal of the irritation leads in these cases to a cessation of symptoms. Cases 2,7,15, and 21 are instances in point.

The usual findings in these cases are polypi, ethmoidal infection, enlarged turbinates, spurs or deviated septa.

CASE 2.

Female Aged 24. Occupation Housewife.

HISTORY.

Attacks of asthma since the age of 10 years. The attacks started immediately after she had an attack of "bronchitis" which she contracted as a result of an exposure to rain for a whole day. Attacks recur irregularly but is always worse during the rainy seasons. No hereditary history and skin tests were negative.

Had tried a large number of different treatments including a course of vaccine injections and all

proved

proved of no benefit. On examination there was a solitary polypus in the left nostril and the nasal septum was deviated to the left. The polypus was removed and sent home with a bottle of a tonic mixture, to report again for further treatment in a week's time. As the patient felt better and no attacks had recurred then, her mixture was repeated and she was to report every fortnight. To the surprise of both patient and myself there was no recurrence of attacks. When I last saw her, she was free of attacks for over one year.

CASE 7.

Male aged 24 years. Labourer.

HISTORY.

Asthma since the age of twelve years. Started after an attack of "influenza". Recurs frequently at intervals of 5 to 6 days. Always subject to a chronic cold in the head. Got douche treatment from several doctors but it never got better. No hereditary history. Skin tests negative. Blood eosinophilia 10 per cent. Examination of the nose revealed polypi and pus. Cure of these led to a complete disappearance of his asthma.

CASE 15.

Male aged 26 years. Shopkeeper.

HISTORY.

Had asthma since the age of 8 years. Attacks occur at irregular intervals and always worse if he gets a "cold in the head". Mother and two brothers are sufferers from asthma. Skin tests gave a positive reaction to bacterial protein. There was

marked

marked septal deviation to the left leading to contact with the turbinals. Septal resection and an out-door hygienic life led to no return of asthma for over one year.

CASE 21.

Female aged 36. Housewife.

HISTORY.

Asthma started at age of 25. She remembered suffering from a chronic cough for years prior to her asthmatic attacks. She was treated by many doctors for that but never got relief and so had given up all hope of a cure. Asthma superseded her cough and she lived a life of misery of over ten years. On examination there was a nasal septal spur in contact with outer nasal wall. This was removed and a tonic and instructions to lead a hygienic life have led to complete recovery when I saw her six months later.

Dundas Grant in 1913 reviewed the literature up to date and (67) stated that in 107 cases of asthma he obtained either improvement or cures in forty five out of fifty nine cases treated for nasal disease.

In 1931 he stated that in 18 asthmatic children in whom (68) were intra-nasal abnormalties in only one did the intra-nasal operation fail to procure some measure of relief.

There is no doubt, however, that the importance of the nasal factor in the production of asthma has often been grossly exaggerated. It must be

remembered that nasal abnormalties are common in a large number of individuals both asthmatics and non-asthmatics.

Becker (quoted by Bray p.115) for example in 360 cases of nasal polypi found asthma in 9. Hering (26) (quoted by Bray p.115) in 200 cases found 7 asthmatic and Schmiegelow (26) (quoted by Bray p.115) in 139 cases 31 asthmatic and in 502 cases of chronic (26) rhinitis asthma in 40.

In the Edinburgh Inquiry of Asthma carried out by Professor M. Lyon and co-workers, (69) examination of the nose and throat of 299 cases of asthma showed that nasal abnormalties were present in 63.1 per cent. Enlarged inferior turbinals were found in 40.5 per cent, septal deviations and spurs were found in 30.7 per cent. Polypi in 15.4 per cent, accessory sinus trouble was noted in 7.2 per cent of the subjects.

To sum up it has been shown that nasal abnormalties occur in both asthmatics and non-asthmatics, and that in many cases radical treatment of such conditions alone may lead to radical cure. It is difficult,however, to say whether the nasal abnormalties are the cause or result of the asthma.

The Nervous or Psychic Factor.

It is a well-proven fact that some cases of asthma depend to a large extent on various psychological states. Thus 75 per cent or more cases on entering hospital without any special treatment

never have any attacks. This is largely due to the belief that they are to be treated by an expert and often that some special form of treatment is being carried out, but it is also partly due, in some cases, to their removal probably from the environment in which they are subject to the exciting allergens. Many cases, however, are on record where the cause has been shown to be psychic in origin. Strauss for example records two cases due to psychic state.(70) One, a boy of 12 years of age who suffered from asthma since the age of three years. Under the influence of hypno-analysis the patient recounted how at the age of two his nurse used to silence his cries by stuffing a rag in his mouth and telling him that if he were naughty a man would come and take him away in a sack. By pointing out to the boy that his attacks were centred round the idea and fear of suffocation the attacks ceased to recur. The other case, a woman, aged 31 years, a school-teacher has recurrent bronchitis since the age of 9. Her doctor diagnosed asthma at the age of 17. Her attacks occurred at night and were invariably preceded by the following dream."I find myself by the side of a brook, quite close to my home. This brook overflows and engulfs me. When the water reaches my neck I awaken into an asthmatic attack." On examination there was a left-sided deflection of her nasal septum and large tonsils. After analysis she had had no return of asthma when she wrote two years later. In this

case there were three other factors present (a) bronchitis (b) enlarged tonsils (c) a deflected nasal septum which might have been regarded as causal and to the elimination of which treatment might have been exclusively and fruitlessly directed. Kholy also reported a case where asthma had supervened (71) on fears of devils and weird things engendered by an ignorant nurse and in which the attacks were cured in three weeks by persuasion and re-education.

Berkart believed that asthma develops upon an endogenous (72) neuropathic basis, the individuals exhibiting from early infancy unmistakable signs of functional disease of the nervous system which is generally inherited. This view is not accepted by many today.

Moos greatly impressed by the efficacy of psycho-analysis (73) in the treatment of the condition believed that the psyche played the chief part in determining the attacks and the whole course of the affection.

In contrast to this view, Bray (p. 102) Hurst and others believe that mental (26) and psychic states (24) can produce allergic responses only in those persons who are already allergic.

Ziegler and Elliott studying the effect of emotion on certain cases (74) of asthma summarise their results as follows:- (1) "Emotion or psychic stimuli seem to induce bronchial asthma in a limited number of people without a history of protein

sensitivity.

2. Patients with a history of asthma associated with psychic stimuli were studied while under the influence of emotion."They demonstrated considerable alteration in the amplitude and regularity of the respiratory curves but little or no changes in rate. The expiratory phase was lengthened and a slight increase in pulse rate was noted.Patients whose asthma was explained on a protein sensitisza-tion basis showed no such changes.

3. In the absence of protein sensiti-zation or a history of the same, a careful study of the relation between emotions and asthmatic attack is indicated and should help to explain the disease in a limited number of patients.

The true position is probably presented by Gillespie who finds that from the psychological point of view,(75) asthmatics fall into three classes. A small group in which the attack has the status as a neurotic symptom. A second group in which asthma is independent of a co-existing neur-osis, but in which emotional causes may precipitate an attack. A third group in which nervous symptoms are definitely secondary to the disability of asthma.

In 1909, Eppinger and Hess (ztchr. f. klin. Med. 1909,67, 345, 68, 205.) called attention to the importance of the vegetative (involuntary) nervous system in certain clinical conditions. They pointed out that many organs are innervated by both sympathetic and parasympathetic nerves and contended that

normally impulses from each keep the other in balance. If, however, the "pull" of one system becomes greater than that of the other, it gives rise to symptoms depending on the organs affected. They based their contentions on pharmacological experiments with pilocarpine and epinephrene. They showed that in small doses, these drugs cause no symtoms in normal individuals but in cases of vegetative nervous system imbalance, they cause exaggerated response, depending largely upon which portion of the system is dominant. Thus in cases of increased vagus tone, or vagotonia, small doses of pilocarpine which stimulates vagus nerve endings will give symptoms referable to the vagus; a feeling of warmth, flushing, sweating; also brachycardia and in asthmatics, paroxysmal attacks.

It has also been shown that heightened irritability of both elements of the vegetative nervous system may occur.

Eppinger and Hess contended that certain clinical conditions could be explained by such vagotonia of which they considered bronchial asthma the best example. Were this a fact, asthmatic spasms should be aborted by the administration of atropine, but such an immediate effect is rare.

The Endrocrine Factor.

It has been often claimed chiefly on therapeutic grounds that the organs of internal secretion bear some relationship to the onset of allergic manifestations. The facts which are put forward

in support of this claim are (1) The rapid and beneficial results of injection of adrenalin in almost all cases.

(2) The occasional beneficial effect from thyroid, parathyroid and pituitary therapy.

(3) The spontaneous recoveries which often occur at puberty.

Hurst (p.5) considers that one biochemical factor[24] operating in certain cases of allergy may depend upon the varying activities of the internal-secreting organs and he explains the effect of fatigue manifested towards the end of each day, the end of each week and the end of each period of work without holiday as due to exhaustion of the supra-renal glands whose deficient secretion helps the vagal constitutent of the bronchial nervous system to gain the upper hand over the sympathetic constituent, the activity of which requires an adequate supply of adrenalin.

Of the endrocine organs, the thyroid gland is the one most commonly blamed. Occasionally one sees beneficial results with thyroid extract therapy, but it is interesting to note that Oehme and Paal (1930)[76] studying the Reid-Hunt reaction in bronchial asthma - a test for hormone in the blood stream and which depends on protection of white mice by aceto-nitril against the toxic action of these substances, found that attacks of bronchial asthma were associated with thyroid excess. Sutherland[77] also describes a case of asthma in which hypo-

thyroidism developed and the asthma was cured and on giving thyroid to remedy the dysfunction asthma again returned.

Ravitch considered thyroid extract a specific for urticaria (78) of the chronic type. In many cases of urticaria associated with asthma I have found thyroid extract of no value to either urticaria or asthma. In fact, it is in this type of cases that treatment by elimination - purgation and diuresis gives encouraging results. Suspicion has also been cast on the sex glands since spontaneous recovery often occurs at puberty especially so in males. In many cases also, in females when the condition begins at puberty recovery often occurs at menopause.

Climate and Locality.

Some asthmatics are better in large smoky cities, while others require the pure country air for relief: some require the hilly country, others flat; and some are free by the sea, others inland. It is difficult to draw conclusions as regards exciting causes because most asthmatics tend to be free from attacks for a variable time after each move.

Climate in its true sense probably participates indirectly only in so far as it affects the growth, production and distribution of certain allergens and favours the development of infections of the respiratory tract and sinuses. In the latter respect it is of etiological importance not only in the causation of asthma but also in the prolongation of the individual attacks and in the initiation of ser-

ious complications which make complete relief from the malady difficult to explain. (p. 174)

According to Adam ("Asthma and its radical (32) treatment" p.179) " place may have little to do with asthma, but the different mode of life, both as to exercise and diet at different places may have much to do with it and give the key to treatment. Place may have much to do with the matter because of two things (a) it may be damp, low lying, relaxing and so depress metabolism (e.g. British Guiana parts of which are below sea-level); or (b) it may be dusty in a general or in a special way, the atmosphere may be dusty from neighbouring works or special pollens e.g. a lady was all right during many months while a cement work was closed and had recurrence of her asthma when they reopened."

Frequency.

The frequency of the condition is difficult to determine but asthma seems to be a relatively common disease in the catologue of human maladies. Spain and Cooke (p. 521) state that three and one half per cent (34) of the American population are subject to hay fever or asthma at some time in their lives. Coca ("Essentials of Immunology" 1925) estimates that 7 per cent of the American population suffer to some degree from hypersensitiveness. According to Coke (79) in England asthma occurs in a well-marked form in perhaps 1 in every 500 of the population. The frequency of asthma seems to vary in different countries but statistics are too meagre

to allow comparisons.

Summary of the Etiological Factors.

Asthma was for many years regarded as a hypersensitiveness due to foreign substances entering the system of the asthmatic. In 1910 Meltzer suggested that asthma was anaphylaxis occurring in man. Later, however, it was observed that asthma was frequently associated with such conditions as urticaria, eczema, migraine, bilious vomiting etc. which are symptoms of the form of hypersensitiveness termed allergy and further observations, clinically and experimentally proved that asthma is an allergic manifestation rather than an anaphylactic phenomenon the existence of which in man is doubted.

The question then arises whether we are justified in assuming that all cases of asthma are allergic in origin. It is generally agreed that this is not so and that no one etiological factor can satisfactorily explain the altered reactivity leading to the protean clinical manifestations one encounters in this mysterious malady. According to Bray (24) (p. 17) "it is by a blending of each of these factors, that the most satisfactory view point is attained." The constant common factor is an inherited, occasionally an acquired predisposition, to manifest hypersensitiveness to various substances, which are generally termed allergens. These may be either specific, or non-specific and may be of an inhalant, ingested, infected or injected nature.

Bray (p. 184) in a study of asthma and hay fever in children in the first decade of life states that (26)
"a positive family history of allergy may be elicited on careful questioning in nearly 70 per cent of cases of asthma, in 50 per cent unilateral and in 20 per cent bilateral. Transmission appears to be twice as frequent through the mother as through the father and the greater the hereditary influences the earlier in life will the symptoms be manifested." In this series a positive family history of allergy was present in 61 cases (52.1 per cent) the average of positive hereditary history obtained from a number of observers who have investigated a large number of cases is about 50 per cent (page 38Table I). In the author's experience , often a patient denies for some reason or other, the existence of asthma or other allergic manifestations in his family and the existence of the malady in the other members, is discovered only accidentally, when another member with the complaint turns up for treatment and is recognised - an easy matter in British Guiana since the medical officer usually gets to know most of the people in his district.

Most observers believe that heredity is a definite factor in asthma and it is generally agreed that the disease itself is not inherited but the predisposition or diathesis is what is transmitted. Biochemical changes have been observed in the blood and urine of asthmatics and these observations

are leading to a better understanding of this mysterious disease. Further research, however, is necessary to determine the significance of these various findings. Adam (Glasgow Hospital Reports 1900,3, 170) stated that asthma is due to toxaemia and that the biochemical changes observed are the results of this toxaemia.

Experimentally, it has been observed that certain bacteria, found in the respiratory and alimentary tract of asthmatics, can produce a substance or substances having a histamine-like action and it has been suggested that absorption of this substance or substances into the system at the part where it is formed, is responsible for some forms of locally produced asthma. The occurrence of histamine in the system and its relation to asthma are still being investigated.

Adam of Glasgow and Haseltine in America claim that asthma (22) is a toxaemia (23) arising partly in the nose and partly in the bowel. They base their contentions on clinical evidence and therapeutic results. Certainly clinically in many cases there are symtoms and signs which point to toxaemia and treatment by "detoxication" gives encouraging results.

Dundas Grant, among others, stresses the nasal factor (67;68) and although one meets cases which get relief from attention to nasal abnormalties only, it is still doubtful whether other factors e.g. psychic are not at work too in bringing about the cures claimed.

The Nervous or psychic factor in asthma has been observed from very early times. The true position is probably presented by Gillespie. Asthmatics fall into three classes. A small group (75) in which the attack has the status as a neurotic symptom. A second group in which asthma is independent of a co-existing neurosis, but in which emotional causes may precipitate an attack. A third group in which nervous symptoms are definitely secondary to the disability of asthma.

Finally there are those who believe that asthma is associated with some endocrine dysfunction. The belief is based chiefly on the beneficial effects of adrenalin injections and the occasional beneficial results of thyroid, parathyroid and pituitary therapy. Further, the spontaneous recovery in many cases observed at puberty is usually attributed to the internal secretions of the endocrine glands.

Treatment.

The treatment of the asthmatic patient naturally divides itself into two parts,(1) the intermediate treatment of the paroxysm.(2) the intensive treatment of the disease during the interval of the attack to prevent further attacks.

The immediate treatment of the paroxysm.

The first step is to relieve the dyspnoea and we can almost always accomplish this by giving an injection of 3 to 5 minims of adrenalin chloride solution 1: 1000 hypodermically. It very seldom fails to bring relief in a few minutes to the true asthmatic and has practically no contra-indications in such doses. It acts by stimulating the broncho-dilator fibres. The dose required to bring relief to the asthmatic sufferer depends on the severity of the attack, the duration of the disease and the patient's previous experience with the drug.

The earlier the injection is given the smaller the dose is required. For this reason we teach intelligent patients to inject themselves since the prompt injection of one or two minims of adrenalin chloride solution at the onset of an attack by the sufferer often wards off an attack. Massage at the site of previous injections of adrenalin, recently recommended we have found of no benefit. In "status asthmaticus" where severe dyspnoea has continued uninterruptedly for days or weeks and fatal exhaustion is feared, the attack can usually

be

be arrested by the continuous method of adrenalin injection advocated by Hurst (p.12)[24]. It consists in leaving the needle of the syringe constantly in position for further injections. After the initial injection of a dose that is known not to cause unpleasant symptoms, one or more minims are injected every fifteen, thirty or sixty seconds, according to the patient's reaction, the rate being varied until it is found how frequently the injection can be made without any unpleasant symptoms arising. The injections are continued if necessary for half an hour or more. This method of treatment nearly always gives relief and the patient usually manages to sleep for the first time perhaps after many distressing days sitting up in bed restless. With this form of treatment chloroform inhalation necessary to bring relief in extremely severe cases should rarely be resorted to.

Morphia in $\frac{1}{4}$ grain doses is a very useful drug at times but its danger is too well known to us to need any further comment. Atropine Sulphate given hypodermically in doses of 1/100 grain to 1/60 grain we occasionally use and it can be used as an adjuvant to adrenalin. It acts by paralysing the terminations of the vagus and should have been the ideal drug in the treatment of asthma if the condition were due to a centrally stimulated vagus and M^{c} Dowall suggests that this drug may be used as a means of differentiating cases of asthma due purely to a nervous origin. Unfortunately atropine alone very seldom brings relief to the asthmatic.

Other

Other drugs we use for their dilator effect on the bronchi are Amyl Nitrite 2 to 3 c.c. by inhalation and nitro-glycerin in doses of 1/100 grain hypodermically. The former causes a rapid dilatation of the bronchi but its action is only short-lived while the latter takes a longer time to act but its action is more prolonged.

Ephedrine introduced in 1923 is a very useful drug in the treatment of asthma. It is an alkaloid obtained from the Chinese plant Ma Huang and has similar pharmacological actions to those of adrenalin and possesses two enormous advantages — it can be taken by mouth and its action lasts longer, from six to eight hours. Further it is very stable and can be boiled without fear of deterioration. In the author's experience ephedrine is the best remedy as a prophylaxis of asthmatic paroxysms. For this purpose, we recommend the drug in doses of ½ grain to 1 grain to be taken morning and evening over a period of 3 to 4 months. The prophylactic treatment of asthmatic paroxysms is of the greatest importance since by warding off attacks it is hoped that the "condition reflex" resulting from repeated attacks and an important exciting factor in many cases may be broken. As a curative we use ephedrine in 1 grain doses two to three times a day and find it very useful. In severe cases, it may fail to bring relief to the sufferer and adrenalin may have to be substituted. Occasionally one meets patients who derive more benefit from ephedrine than adrenalin, in other words ephedrine is

tolerated

tolerated better than adrenalin by these patients. The disadvantages of ephedrine are (1) it takes longer to produce its effects usually about half an hour if taken by mouth or ten minutes if administered subcutaneously. (2) some patients experience unpleasant symptoms such as palpitation, giddiness, headache and tinnitus after its use even in small doses.

Ephedrine is now prepared synthetically and is sold under the name of ephetonin. Stimulants we use, when patients show any signs of exhaustion and the ones, we use most, are strong coffee or alcohol. These sometimes act like a charm inducing sleep and bringing some relief. Diet should be light and nourishing. In fact, during the attack patients have no inclination for food and no attempt should be made to push it since the presence of food in the stomach often aggravates the symptoms. Attention to the amount of fluid intake is of the greatest importance. It is surprising to know how little fluid these patients take and it is essential that a sufficient amount of fluids be taken. If the patients cannot take fluids by the mouth we always give a glucose saline enema.

If the patient shows no signs of exhaustion, on first seeing him, we give calomel grains 3 following by magnesium sulphate four hours after.

Sprays are frequently recommended but we use this form of therapy only among private patients. The disadvantage is that the apparatus required for their administration is generally cumbersome.

The

The apparatus most highly praised by patients is the "Apneu" inhalation apparatus. By means of this oxygen is made to spray adrenalin and stramonium into the air breathed. In many cases the attacks are warded off by this form of therapy. Tucker's Spray is also much used. It contains cocaine (1 per cent) together with potassium nitrate (5 per cent). Recently Hurst has advised the inhalation of carbon dioxide directly into the nose as a sedative to the nasal irritation and rhinorrhoea that sometimes precede an attack.

Inhalations, powders and cigarettes are much used by asthmatics. In fact, there are few chronic asthmatics who have at some time or other, not tried this form of therapy. These generally contain potassium nitrate and the dried leaves of Datura Stramonium. The fumes are inhaled and benefit is due to the nitrites produced from the nitrate. This form of treatment we do not recommend but rather discourage their use among patients, since the relief is only temporary, an unpleasant smell hangs around the place for some time and most important of all, they have an extremely irritating effect on the bronchial mucous membrane, which in turn increases the liability to further attacks. Emetics such as Vin. Ipecacuanhae in ½ to ¾ ounce doses or Vin. Antimonalis in ¼ ounce doses or Apomorphine Hydrochloride in doses of 1/10 grain to ¼ grain by mouth or 1/20 grain to 1/10 grain hypodermically is occasionally useful but we never use this treatment as a routine procedure.

Various

Various medicines are usually prescribed. Most are antispasmodics and help to some extent in relieving the paroxysms. Those commonly employed are various combinations of potassium iodide, Tinct lobelia, Tinct Stramonium and Tinct belladonna. The Mixture found most useful by the author is the following:-

℞ pot. Iod. grains X

Tr. Lobel aether.

Tr. Stramonii āā minims X

Tr. belladon.

* Liq. Morph. Hyd. āā minims V

Spt. Ammon. Aromat Minims XV

Aq. Camph. ad Ounce ½.

Sig. ½ ounce 4 hourly.

* This is added only in very severe cases.

Aspirin in doses of 5 to 10 grains is frequently effectual in controlling an asthmatic attack, and among patients it is one of the most common home remedies for all ills. It must be remembered, however, that aspirin is the commonest form of drug hypersensitiveness encountered in allergy and for this reason we do not recommend its use generally. Sodium Iodide intravenously has been advocated for asthma, particularly by proprietary concerns interested in the preparation of intravenous products. Iodides are rapidly absorbed when taken by mouth and we therefore never use it intravenously in asthma. Pituitrin alone or in combination with adrenalin (asthmolysin) is highly recommended as a cure for asthma by a few physicians. It is generally admitted, however, that without the adrenalin it is

of

of questionable value.

Arsenic by mouth is of no use in the treatment of a paroxysm but when given over long periods of time, it is said to have a favourable influence upon the bronchitis and asthma.

The treatment of the paroxysm, although merely palliative, is of the greatest importance, as, if successful, it may make it possible for a man to continue in full activity instead of becoming a hopeless invalid.

Intensive treatment of the asthmatic during the interval of an attack.

The first thing to do is to determine, if possible, the exciting cause. When this is some food, flowers, or pet e.g. cat, dog, rabbit, or parrot, then the matter is a simple one and the removal of the offender results in cure. Unfortunately it is only in a few cases that this is possible. However, the result of a thorough investigation will point to the most hopeful lines of treatment for each individual.

In every case, the general hygiene of the patient should receive fore-most attention. The bowels should be opened by salines, or by calomel and salines, on first seeing the patient, provided he is not too exhausted. If, however, the patient is weak perhaps a simple enema may be best. Orange juice and fruits, easily and cheaply secured in the tropics, should be recommended and a habit to move the bowels daily without the aid of purgatives should be patiently cultivated. Patients naturally

dislike

dislike taking purgatives and some often prefer to allow the colon to become loaded for a day or two rather than have a daily dose of cascara or magnesium sulphate. Constipation, apart from whether its role in the etiology of the disease, is by reflex action or by producing toxaemia, certainly leads to ill health after a time and tends to aggravate any pathological process that is already present. Plenty of fresh air and minimum of furniture in the patient's room should be aimed at. Regular exercise and light nourishing diet are recommended. Heavy meals in the evenings should be strictly banned. Every effort should be made to combat any tendency to flatulence or constipation since gastric and rectal distension commonly precipitate an attack. In cases of hypochlorhydria, hydrochloric acid is indicated. The dose recommended is ½ to 2 drachms in a cup of orange or lemon juice thrice daily before or with meals. Bray finds that in children, this therapy, if continued for some months, in a majority of cases, leads to an increase in weight, better appetite, sounder sleep and a cessation of attacks. The prescription he employs in children is as follows:- (49)

℞ pepsin 1 grain
Ac. Hydrochlor. dil. 30 minims
pure Dextrose 30 grains
Syr. of Senna 10 minims
Aq. Chlorof. ad 2 drachms

Sig. Two teaspoonfuls in orange or lemon juice three times a day before meals.

For children he finds that 5 minims of adrenalin chloride

chloride solution added to this prescription, appears to have some action, contrary to accepted opinions that it is not absorbed by mouth. The pepsin mixture should be recently prepared, as with age, large amounts of hydrochloric acid tend to destroy the activity of the pepsin. If there is a concomitant chronic gastritis, thorough mastication and in resistant cases, gastric lavage every morning with a dilute solution of hydrogen peroxide will relieve the symptoms. In the tropics, helminthic infection should be sought for and treated. Ascaris lumbricoides infection is very common in British Guiana and the author has seen cases of dyspnoeic attacks, recurring periodically, due entirely to Ascaris lumbricoides infection, since in every case eradication of the infection resulted in cure of the attacks of dyspnoea. The periodic attacks of this dyspnoea apparently occurs whenever the worms have accumulated in great number in the alimentary tract or reflexly cause irritation of the diaphragm since in many of these cases, vomiting of one or more of these worms occur simultaneously with the dyspnoea, and this usually gives relief. Often it is the first sign indicating the diagnosis.

In all cases, on first seeing the patient, his ear, nose and throat should be examined by an expert if possible. Infection and other causes that may produce irritation in these parts should receive treatment since an asthmatic attack can be produced reflexly by irritation of the nose or ear. It must not be forgotten, however, that nasal abnormalities

are frequently a complication or sequel of asthma and that treatment directed primarily and solely to the nasal condition will not result in relief of these cases. Dundas-Grant has claimed extremely favourable results from nasal treatment operative (67) and otherwise of cases with nasal abnormalities. On the contrary, Rackemann and Tobey report that only a small percentage of their large series of cases (80) were completely relieved of asthma by nasal operation . Again Lyon and Murray-Lyon in a review of the results of treatment in 291 cases of asthma (25) concluded that the results of operations on the nose or throat are disappointing, and such treatment should only be recommended to relieve definite local symptoms.

Operative interference should certainly only be advised to relieve definite local symptoms e.g. the presence of definite localised sepsis or of definite obstruction to nasal breathing. Thus pus in the ethmoidal air cells or maxillary antra demands energetic treatment. Again nasal polypi are prone to aggravate the asthmatic symptoms by direct obstruction and by reflex irritation and they should therefore be removed. When, however, there is merely a deflected septum, a well-balanced judgment is a necessity, if patients are to be spared unnecessary operations. The mere deflection of a nasal septum is so common that it might indeed be regarded as normal for some races. Marked septal deflection, sufficient to obstruct breathing and to bring the septum and middle turbinal into contact , permanent-

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ly or at times of congestion should, however, be corrected. Such a state of affairs will give rise to pathological stimulation of the spasmogenic area of the septum or the obstructed air may lead to mouth breathing especially at night when the patient is asleep. This, in turn, will produce sore throat and aggravate any existing bronchitis. Conservative treatment should be the slogan in dealing with the turbinates since their function is to warm and moisten the inspired air. Cauterization of the sensitive area of the nasal septum is often recommended but only temporary improvement occurs in some cases and permanent benefit very rarely. Other sources of focal sepsis should be sought for and corrected. Thus carious teeth and pyorrhoea should be dealt with without delay. Sepsis in any part of the system will doubtless adversely affect the progress of asthma, what-ever methods of treatment are employed.

Skin tests may indicate hypersensitiveness to one or more substances and removal or avoidance of contact with these by the patient will often result in cure. Thus if the patient give positive reaction to dog or cat hairs removal of these animals and all trace of their hair from the home may result in cure of the asthma. Again some offending foodstuff may be detected by skin tests and removal may result in a cure. In other cases in which the specific causes cannot be removed or avoided desensitisation should be attempted. This will be dealt with later. In some cases, there may be indications of

endocrine

endocrine dysfunction and in such cases, endocrine therapy should be tried. The author has seen two cases of asthma where there was only the slightest suggestion of hypothyroidism benefited by thyroid extract therapy. On the other hand, in many cases where this drug was tried no benefit was noted. The parathyroid, pituitary, thymic, supra-renal and sex glands have all been blamed. In some cases some benefit is noted by therapy with extracts of these glands, more frequently, however, no benefit is derived from their administration.

Again one must always keep in mind the mental side of the disease. The mental suffering of patients during the severe paroxysms, when the sensation of suffocation and imminent death produces a feeling of absolute terror -- especially in children -- leaves them in a state of chronic fear. Dread of an attack plays some part in its production, and one should therefore as far as possible divert the patient's thoughts from himself. It is a fact that the majority of patients become either completely or almost free from symptoms directly they enter a hospital. This is often due partly because they have got away from the exciting factors which are present in their homes or environment and which were responsible for some of their attacks and partly, in fact sometimes entirely, due to the expectation that they are going to derive benefit from the treatment they are about to receive. For this reason, one should always instil a spirit of optimism into asthmatics and make them realize that

improvement

improvement may at any time occur and that conditions which formerly gave rise to asthma may cease to do so. Hurst (p.10) believes that in this way alone can the influence of expectation in the production of attacks be overcome. (24) In some cases even gross suggestion sometimes proves beneficial. Hurst described a case with severe status asthmaticus who could only get relief after injection of (24) ¼ grain of morphia. His house physician, however, got equal relief when water was substituted for the morphia, the relief being not merely subjective, but accompanied by an immediate and complete disappearance of the physical signs indicating severe spasms of the bronchi. Again, sometimes, when all other methods of treatment fail, psycho-therapy succeeds. Moos claims marked benefit from psychoanalysis. (73) He advised treatment conducted for at least an hour weekly over a period of six to eight weeks. At the commencement of treatment Moos seldom found it possible to cut short an asthmatic attack by hypnosis, but as treatment progressed suggestion became increasingly effective.

Desensitisation.

In those cases in which the specific causes cannot be removed or avoided entirely, one should attempt to desensitise the patient. The methods employed may be either specific or non-specific in nature. The principle consists in applying just enough stimulus by some allergen or other substance to use up the reactivity or reduce or exhaust the cellular allergin.

Specific

Specific desensitisation is the term employed when the definite causative allergen is used, or, where there are multiple reactions, the largest of each group may be combined.

There are various methods by which specific desensitisation may be accomplished, thus, by giving gradually increasing doses of the allergen, by the mouth desensitisation may occur. This may be tried when the allergen is a common food. Again by producing cutaneous reactions repeatedly, by intradermal injections, desensitisation sometimes occurs. The commonest and most used method of producing desensitisation is, however, by the subcutaneous injection of the allergen in gradually increasing doses. By this method, desensitisation to animal emanations, orris root and dust may be accomplished either by the "rush" method devised by Freeman for pollen allergy (81) or by the more lengthy weekly method. In either case a series of dilutions of the offending hair or dust is prepared. In cases of multiple sensitisation the hairs are kept together and so are the dusts and powders, and they are injected separately. The strongest solution, that can be prepared, is obtained and is known as "A". From this dilutions are made and those of 10 are called "B", 100 "C", 1,000 "D", 10,000 "E", and 100,000 "F". Lower dilutions than this are rarely required. The "rush" method is carried out as follows:- The skin is tested with solution "F" intradermically and if no reaction is obtained in five minutes, the same procedure is adopted with solution "E", "D" or "C" until

until a positive reaction is obtained about an inch in diameter using 1/20 c.cm. intradermically. Say "D" is the solution that just produces this desired effect, treatment is commenced with 0.1 c.c subcutaneously at 8 A.M. and increased by 0.1 c.c. each second hour till 10 P.M. at which time the dose is 0.8 c.cm. Next morning the same procedure is carried out with solution "C" which is ten times stronger and next day with solution "B". As the dose gets larger the local reactions become more pronounced, when it is advisable to repeat the same dose for one or two injections, using different parts of the body. In from five to seven days it is usually found that the patient can stand large doses of solution "B" with impunity. Usually the patient is taken into hospital for five to seven days and after this time is returned to his previous occupation or residence. Sometimes the sufferer remains free and no further immediate therapy is required. At other times, after a varying internal, there is a relapse to a mild degree, when the injections may be continued weekly with increasing doses of the stronger solutions. The method of weekly subcutaneous injections is more commonly used and more usually for mild cases. The dose is double the previous -- 0.1, 0.2, 0.4, 0.8 c.c. of each solution until the local reactions tend to be large, when each succeeding dose is only increased by 0.1 c.c., but injections may be given every 3 days. Usually the course of injections occupies about three months.

Recently

Recently "proteose" has been isolated from the urine of the patient and used for specific desensitisation. Beneficial results have been claimed by some observers who have carried out treatment with this substance. The treatment is too recent yet to allow any definite assessment of its value and there is some doubt as to its specificity.

The great objection to specific desensitization is the length of time and expense involved, and the uncertainty of effect even if every precaution has been taken.

If no specific allergen is detected as the cause of the asthma, desensitisation may be attempted by various substances, i.e. non specific desensitisation. The principle adopted, is to endeavour to use up the reactivity of the patient with another protein in the hope that it will counteract the reactivity to the specific protein. The methods we employ at Suddie are with peptone, tuberculin, milk and vaccines.

Peptone.

The use of this substance was advocated by Auld in 1917 in the treatment of bronchial asthma. (82) He used Armour's peptone in preference to Witte's peptone as he believed the latter was unfavourable on account of the histamine it contained. Other workers, however, prefer Witte's peptone. Again some give it subcutaneously, while others give it intravenously, and others yet intramuscularly. We usually give peptone intravenously at Suddie, starting with 5 minims of a 5 per cent preparation.

Injections

Injections are given twice weekly and the dose is gradually increased and regulated according to the reaction of the patient. The reactions are occasionally very severe and the dosage must be carefully regulated as marked bronchospasm and fatal results may occur. About twelve to fifteen injections complete the course. This, in the author's hands, gives good results in some cases and is worth while trying in selected cases. According to Auld, suitable cases for peptone therapy are patients having favourable intervals, with freedom from bronchitis and much emphysema. The more recent the disease and the more regularly spaced the intervals, the better the result. Young patients do very well.

Tuberculin.

The treatment of asthma by tuberculin was introduced by Storm van Leeuwen and Varekamp in 1921. (83) The method consists in first testing the sensitiveness of the patient by an intradermal injection of 1/10 c.cm. of a 1 in 1,000 dilution. A strongly positive reaction indicates an initial dose of 1/10 c.cm. of 1 in 1,000,000 dilution of old tuberculin subcutaneously. The injections are given every two days, rising by 25 to 50 per cent, but after two weeks they are given at five days intervals, and subsequently once a week. When the actual value to be injected reaches 1 c.cm., a stronger solution is employed, with corresponding reduction of dose.

For patients who show but a trivial reaction to the skin

skin test, a 1 in 100,000 or 1 in 10,000 solution may be used from the start. The treatment should extend over six months at least and should not be given in cases where active tuberculosis is present. Storm van Leeuwen reports cures or great benefit in over 75 per cent of cases subjected to tuberculin therapy.

Ling (1928) Simpson and Stone (1929) and Max-well (1930) have all obtained good results with tuberculin therapy in a small number of cases.[84] [85] [86] The author, in a small number of cases, in which this treatment was tried, found it of value, but it was difficult to determine how much of the benefit was due to the tuberculin and how much to the psychological effect of frequent stabs with the needle. In many of the cases, relapse occurred and patients soon get tired of repeated injections.

Milk.

Schiff in 1923 was the first to suggest the injection of whole milk as a means of inducing protein shock in the treatment of asthma.[87] The method consists in sterilising two ounces of whole milk in a rubber-capped bottle. Injections are given thrice weekly beginning with a dose of ½ c.cm. and increasing by ½ c.c. until 3 c.cm. doses are reached. This treatment is not advised for milk sensitive cases. The advantage of this method of treatment is its low cost, and it seems to give just as good results as other forms of non-specific desensitisation.

Vaccines.

Vaccine therapy is employed in a large number

of

of diseases and on the whole with disappointing results. In asthma, however, quite a number of patients appear to derive some benefit from its use. This is especially so among patients whose asthma appears to be secondary to catarrhal infection of the respiratory tract. In 1913 Pirie (B.M.J. 1913,1,1268) reported 9 cases of asthma treated with autogenous vaccines, -- 2 were cured and 5 considerably relieved. In 1917 Montgomery and Sicard (Am.J.Med.Scien.1917,53,856) reported as cured 12 out of 16 cases of asthma treated with autogenous vaccines.

In 1924 Veitch (B.M.J. 1924,1,13) recommended combined peptone and vaccine therapy in the treatment of asthma. Of 24 cases treated he reported that 14 were cured and 9 greatly improved.

In asthma either an autogenous or a stock vaccine may be used. Some claim best results with an autogenous vaccine prepared either from the patient's sputum or from a throat swab, but in the author's experience a stock vaccine containing a mixed flora gives just as good results. The initial dose should be 1/10 c.cm., subsequent doses rising by 25 per cent increments unless constitutional reactions indicate a modified procedure. Injections should be given every 5 to 7 days and usually a course of 12 to 15 injections should be given and repeated if necessary after a rest interval of 8 to 12 weeks. Should an attack of acute bronchitis, coryza or influenza occur in the course of treatment, injections must be suspended until recovery has taken

place

place. The next dose must then be reduced to at least half of that which preceded the acute infection.

T.A.B. Vaccine intravenously, sometimes brings relief to cases in which other methods of treatment fail. The initial dose is usually 25 million organisms. This is gradually increased, depending on the patient's reaction, and injections are repeated weekly. Its beneficial effect apparently is due to protein shock.

Diathermy.

Hall (1930) advocates the use of diathermy, a high-frequency current (87) of the alternating type in which the oscillations have been steepened up to the neighbourhood of a million a second. Heat is generated in the tissues by their resistance to the passage of these oscillations and it is this heating which is said to have a soothing effect as well as a possible bacteriological one, in addition to assisting in the repair of inflamed or damaged organs or tissues.

Treatment by diathermy alone never results in cure of asthma but it is a very useful adjunct to other therapeutic measures in those patients whose attacks originated from a respiratory infection (Douthwaite on treatment of Asthma p.125).

X-Ray Therapy.

In 1906 Schilling reported the first case of asthma treated and cured by radio-therapy. This method of treatment may be tried in cases where no reason has been determined for the asthmatic

seizures

seizures, or in which desensitisation therapy has failed. It is doubtful how these irradiations act. It has been suggested that they reduce glandular enlargements, have a sedative effect on the nervous system, a regulative effect on the endocrine system, or an effect similar to non-specific desensitisation due to repeated minute doses of substances entering the circulation from the breakdown of cells altered by the passage of the rays. Some have applied the rays to the thoracic region and particularly the hila, believing the asthmatic attacks occurred coincidently with enlargement of the tracheo-bronchial glands, the diminution of which caused a cessation of attacks. Others have applied the rays to the spleen with the idea that the production of antibodies would be stimulated. Others have combined the irradiation of both hila and spleen.

Ultra-Violet Rays.

It has been advised that these rays, applied both locally to the chest and generally to the body and limbs, are useful in the treatment of asthmatics. The various sources of these rays employed in treatment are sunlight, the quartz mercury vapour lamp, the tungsten or carbon arc lamps. Hall advises general body exposures once or twice a week (87) in gradually increasing amounts, the initial dose being a two minutes' exposure at a distance of 3 feet from the mercury vapour or tungsten arc lamp. The duration of treatment should not exceed three months followed by a 6 to 12 weeks' halt. The dose must

must be regulated according to the reaction of the patient. Hall (p.106) believes that ultra-violet radiation has the power to bring about a general desensitisation of the patient to the various exciting agents which provoke the paroxysmal attacks of asthma. (87)

Medicinal Treatment.

Of other drugs used in the treatment of asthma, mention must be made of calcium. It was believed that in asthma there was a deficiency of calcium in the blood but further investigation has not confirmed this belief and again the administration of calcium lactate by mouth is found of no benefit. Some believe that the active blood calcium may be deficient in asthma and in order to raise this they recommend 30 grains of calcium lactate daily combined with ultra-violet radiation or with irradiated ergosterol e.g. radiostoleum or vigantol in 10 minim doses twice daily.

Glucose has been advised by Oriel, who has found hypo-glycaemia in a majority of cases of asthma. He recommends 2 ounces of the powdered dextrose dissolved in water and flavoured with orange or lemon juice night and morning on an empty stomach. Barber and Oriel also recommend the administration of ammonia in the form of sal volatile in doses of half a drachm in water thrice daily before meals. The idea arose from the observation of the increased ammonia excretion and acidosis. (38) (41)

Arsenic in the form of Fowler's solution, Bray states, is of value at times especially in children. (26)

The

The author has found intravenous use of arsenic in the form of neo-arsenobillon of great benefit in adults. In fact, in many cases in which all other forms of treatment fail benefit has been obtained by the intravenous exhibition of this drug. The disadvantage is that severe reactions may occur.

Surgical Treatment.

Besides the removal of septic foci and nasal growths and deviations, other surgical measures that have been recommended are bronchoscopy and neurectomy. Such treatment, however, is restricted to the specialist and their therapeutic value is questionable.

Physical Exercises and Massage.

Remedial exercises are recommended in all cases of asthma in which the attacks follow each other so rapidly that the over expanded lungs do not have an opportunity to return to their normal size and as a result of which the thorax assumes the so-called barrel shape, the shoulders shrugged, the spine unduly curved, and the epigastric angle wide. During the inter-paroxysmal periods, it will be remembered that the patient tends to hold himself tensely and rigidly and the thoracic muscles assume a new postural length and tone. The object of physical treatment is to restore mobility and flexibility to the thoracic parietes; to teach the patient general muscular relaxation; to guide his respiratory movements with a view to re-establishing a normal rhythm; to assist in the expulsion of air from the pulmonary alveoli and finally massage is applied to

the

the limbs in order to aid the venous circulation and prepare the body for active exercises. Various schemes of exercises have been advised by several workers in this field. (89 and 90)

A masseuse is necessary for the guidance of patients in the carrying out of these exercises and as there is no masseuse in any of the hospitals in which the author worked, this form of treatment was not carried out.

SUMMARY AND RESULTS OF TREATMENT.

From a perusal of the preceding pages it will be seen that each case requires careful investigation and study and the exact method of treatment adopted will differ according to individual indications. Each patient requires advice and treatment along hygienic lines. The most successful forms of therapy is by elimination where applicable. In all types of asthmatics, careful regulation of the quantity and quality of the food and the times of food intake will amply repay the trouble.

Elimination of focal sepsis and suspected sources of reflex vagal stimulation is of great importance, since sepsis and irritation of the vagus tend to aggravate any pathological process present. The results of such treatment, however, from the point of view of permanent cure, is seldom striking. Rackemann and Tobey, and Lyon and Murray-Lyon (80) reviewing the results of treatment in a large series (25) of cases are of the opinion that the results of operation on the nose or throat are disappointing, and advise that such treatment should only be recommended to relieve definite local symptoms.

Vaccine therapy in suitable cases is often highly efficacious.

Specific and non-specific desensitisation is, as a rule, disappointing in the results obtained.

Actino-therapy, diathermy, X-Ray and psycho-analysis can all be useful but chiefly as adjuvants to other more radical treatment.

The majority of drugs are of use merely to hold

symptoms

symptoms in check and probably have no value in eliminating or correcting the asthmatic tendency. Permanent residence at high altitudes is said to abolish the paroxysms in nearly every case but it is not to be recommended in the presence of bronchitis of any severity. Furthermore, the number of patients who can avail themselves of such an opportunity is necessarily restricted.

Physical exercises and massage cannot cure the asthmatic, but can and do materially retard the development of organic changes and lengthen the inter-paroxysmal interval. They should, therefore, be employed in all but the mildest cases. Unfortunately no systemic exercises were carried out in the author's field of work as there is no trained masseuse connected with any hospital there.

CONCLUSIONS.

1. Asthma is a comparatively common disease in British Guiana.

2. Clinically, asthma can be divided into two types, one termed primary for convenience and in which there is usually a family history of asthma, hay fever or allergic manifestations such as eczema, urticaria, cyclic vomiting or migraine. This type usually begins in childhood. The other, termed "secondary", usually follows some respiratory affection e.g. measles, whooping cough, bronchitis or pneumonia and usually starts in later life. Oriel and Knott (38) (39) have found in these two types biochemical differences which tend to support this clinical differentiation.

3. In the diagnosis and treatment of the condition, Ascaris lumbricoides infection must be kept in mind and stool examination for eggs of this helminth should be practised as a routine in all cases of asthma in the tropics if only to exclude this condition.

4. A number of factors probably operate in the production of this malady. The one constant factor appears to be an inherited diathesis or predisposition, though in some cases this predisposition may be acquired. Other factors such as allergy, toxaemia, reflex irritation, psychical disturbances, biochemical changes and endocrine disturbances all may play their role in the production of this distressing disease. Only time and experience will determine the relative merits of each.

5. Early treatment is of the greatest importance.

6. No one treatment is applicable to every case of asthma. Each case requires thorough investigation and individual treatment.

7. The most successful form of therapy is by elimination, when applicable.

8. If the specific cause cannot be eliminated or avoided, specific desensitisation should be attempted.

9. If the specific cause cannot be determined, recourse must be had to non-specific desensitisation with peptone, milk, tuberculin or vaccines. It is always worth while trying different forms of treatment since in many cases where one form of therapy fails another may succeed.

10. Psycho-analysis and endocrine therapy may be indicated in individual cases.

11. In adults, arsenic in the form of neo-arsenobillon intravenously the author has found of benefit and often succeeds where other methods of treatment fail.

Lastly, I am indebted to Professor D.M. Lyon for permission to investigate the cases collected from his wards and for helpful suggestions and also to Dr. Chalmers Watson for permission to gain access to his case records.

APPENDIX.

A.

ANALYSIS OF TABULATED CASES.

In the following tables one hundred and seventeen cases are analysed. Seventy eight of these were personally examined and thirty nine are cases of asthma admitted to ward 28, Royal Infirmary Edinburgh during the years 1919 to January 1932.

The sample here analysed is open to objection for the following reasons.

(1).The fifty five cases examined in British Guiana are not consecutive cases but more or less selected from a large number of cases which have come under the author's observation.

(2).Of the cases collected and examined in the Royal Infirmary Edinburgh the proportion of patients under ten years is less than might be expected since most young children in that area are dealt with in a special hospital.

The record shows the number of cases in the successive decades of life as follows;-

Under 10 years	14
From 10 to 20 years	31
" 20 to 30 "	16
" 30 to 40 "	21
" 40 to 50 "	14
" 50 to 60 "	16
" 60 to 70 "	4
" 70 to 80 "	1
	117

Thus it is seen that the number of asthmatics are greatest between the ages of 10 to 20 and between 30 to 40. In the other age periods the number of cases is fairly uniform but over 60 the numbers rapidly diminish.

Age of first appearance of asthma.

Asthma may start at any age period of life. In the following table the age of onset in this series is shown.

TABLE II.

SHOWING AGE OF ONSET IN DIFFERENT AGE PERIODS.

YEARS.	TOTAL.
0 to 10	44
10 to 20	17
20 to 30	20
30 to 40	16
40 to 50	10
50 to 60	7
60 to 70	3
	117

It will be observed that the largest number of cases 44 (37.6 per cent) occur in the first decade of life. This is in agreement with several other observers. Thus Hyde Salter (p.113) reported 71 (31.5 per cent) of his 225 cases occurred in this period.while Adam (Asthma and its radical treatment p.132.) gives over 40 per cent as commencing during the first ten years. Again Bray (15) (p.182) (26) states that one third of all cases of asthma start during the first decade and in one out of every

Coke (B.M.J. 1927, 1, 955) found 41.1 per cent in 1000 cases started in this period.

four such suffers the onset will date from the first year.

Sex.

In this series there are 70 males (59.83 per cent) and 47 females (40.17 per cent). A preponderance of males.

In the following table is set out the number of males and females in the different age periods.

TABLE III.

SHOWING MALES AND FEMALES IN DIFFERENT AGE PERIOD.

YEARS.		MALES	FEMALES.
0 to 10	...	31	13
10 to 20	...	8	9
20 to 30	...	11	9
30 to 40	...	7	9
40 to 50	...	6	4
50 to 60	...	5	2
60 to 70	...	2	1
		70 +	47 = 117

Between the years 0 to 10, there were 31 males and 13 females; after the age of 40 there was a slight preponderance of males over females while in the other age periods, the proportion of sexes was about equal. Hyde Salter (p.114) gives a two to one preponderance of males to females.(15) Bray (p. 183)(26) also gives a similar preponderance of males to females up to the age of puberty and from then on to the menopause, a slight preponderance of females and in old age there is again a slight preponderance of males. In this series there were 36 males

and 17 females up to the age of 15 years (age of puberty). From the age of 15 years to 45 years (age of menopause) there were 25 males and 25 females, the sexes being equal; and from 45 to 70 years there were 9 males and 5 females, a slight excess of males.

Assigned cause of onset.

In this series, in 76 cases the assigned cause of onset of the condition was noted; in 34 cases bronchitis was blamed; in 11 pneumonia; in 6 measles; in 5 influenza; in 4 whooping cough; in 5 urticaria or eczema; in 4 gastric disturbances; in 3 cold in the head; in 2 injury; in 1 pregnancy; in 1 removal of tonsils and adenoids; in the others, the cause was not stated or known.

TABLE IV.

SHOWING ASSIGNED CAUSE AND NUMBER OF CASES.

ASSIGNED CAUSE.	NUMBER OF CASES.
Bronchitis	34
Cold in the head	3
Pneumonia	11
Measles	6
Influenza	5
Whooping Cough	4
Eczema or Urticaria	5
Gastric Disturbance	4
Injury	2
Pregnancy	1
Removal of Tonsils & Adenoids	1
Not stated or known	41
	117

Thus in 63 cases (53.8 per cent) the condition was attributed to some affection of the respiratory tract or some acute infectious disease e.g. measles or whooping cough in which bronchitis or other lung affection is a common complication.

Baldwin (J.Allergy 1929 to 1930,1,124 cited by Bray in Recent Advances in Allergy p.184) has carefully studied the stimulus leading to the first attack in a series of twenty five cases and has found that it was either a specific protein or an infection involving the respiratory tract. It was found that further attacks could be induced by the same stimuli or by a hetereogeneous group of non-specific excitants, including emotion and psychic factors, exertion, and altered atmospheric conditions.

Bray (p.184) thinks that there are three means (26) by which the relationship between infection and allergy may be evidenced. "First, an acute infection often ushers in the sensitive period in an allergic person, the dormant allergic state becoming active during the period of lowered resistance. Secondly, in many cases it appears that, in the absence of any hereditary taint, a definite sensitivity develops to some allergen during the damage state of the mucous membrane. Thirdly, by reason of his allergy, an allergic person may be more susceptible to the inroads of infection, invading micro-organisms thriving in the lowered resistance of a mucous membrane constantly irritated by specific protein."

Premonitary Symptoms.

Premonitary Symptoms.

These were noted in 75 cases (63.1 per cent). The importance of these is that if they precede the paroxysms several days or possibly as long as months, as the author believes occurs in some cases, then there is a chance for such patients to obtain treatment in the pre-paroxysmal stage, so to speak and have a better chance of completely eradicating the complaint. In the few cases of this kind that the author has seen, the results of such early treatment has been very striking. Case 8 quoted in this thesis (p. 49) is an instance in point. Although it must be admitted that such cases are not frequently seen, yet it is interesting to note that Lyon and co-workers have also observed in one or two of their subjects (69) a similar occurrence - prodromal symptom in the form of a choking sensation of a few minutes duration on exposure to an irritant, with a fully developed asthmatic spasm during the following night. The majority of asthmatics that attend hospital are cases in which asthma has existed for years and for this reason it is often very difficult for them to recollect the early symptoms associated prior to the fully developed paroxysm. Only further observation and careful enquiry will determine if such important and early manifestations of the disease are at all common.

Heredity.

In this series, some close relative had suffered from asthma or hay fever in 61 cases (52.1 per

cent) of the number of patients examined. Bray states that "a positive family history of allergy may be elicited on careful questioning in nearly 70 per cent of cases of asthma, in 50 per cent unilatereal and in 20 per cent bilateral. Transmission appears to be twice as frequently through the mother as the father, and the greater the hereditary influences the earlier in life will the symptoms be manifested. The factor toward which a definite sensitivity is developed generally depends upon the environment."
This factor has already been discussed under the etiology of the disease.

Skin Tests.

The results of these (the scratch method being employed) were on the whole disappointing. 73 cases were tested and in only 18 cases (25 per cent) was the test positive. Further in only 5 cases (7 per cent of the number of cases tested) were the tests compatible with the patient's history e.g. if the patient gave a positive reaction to eggs and milk and could take these with impunity during the intervals of the attacks, the test was more or less disregarded.

Blood Count.

In 30 cases of this series blood count was done and in all of the cases there was an increase of four or more per cent. Adam (B. M. J. May 1932 p. 973) states that "wheeze plus eosinophilia is asthma."

The significance of the occurrence of eosinophilia in asthma is still, however, a debatable point.

Treatment.

In this series 13 cases received neo-arsenobillon intravenously, when other forms of treatment had failed to benefit, and the results were as follows: 4 had no recurrence of symptoms, seen or reporting many months after treatment; 6 were improved by which is meant attacks had diminished and the general bodily health of the patient had improved; and 3 showed no improvement. The value of other forms of treatment has already been commented on.

TABULATED CASES.

Number. Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia.	Treatment	Remarks.
1. F; aet.56. Housewife.	"Cold in the chest."	44 yrs.	Polyuria and oppression in chest.	Father and Cousin suffer from asthma.	Negative.		Symptomatic; Vaccines.	Improved.
2. F;aet.24. Housewife.	"Bronchitis."	10 yrs.	None.	NOne.	Negative.		Removal of polypus and a tonic mixture.	No recurrence during 1 yr.after.
3. M;aet.13. Messageboy.	"Pneumonia."	5 yrs.	Flatulence.	Sister and Brother asthmatic.	Negative.		Other treatment and then injections of neoarsenobillon.	No recurrence 11 months after last injection.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
4. F;aet.12 years. School-girl.	Measles.	5 yrs.	None.	Maternal grand-mother asthmatic.	Negative.		Initial purgation, hygienic life, avoidance of constipation, and diuretics.	No further attacks of asthma for 6 months.
5. F;aet.1yr. Nil.	"Cold in the chest".	8 yrs.	Drowsy and depressed.	Maternal grand-mother asthmatic.	Wheat and eggs +	12% (During interval).	Avoidance of wheat and eggs, Hygienic measures and diuretics.	Improved.
6. M;aet.52 years. Labourer.	"Cold in the chest and fever".	10 yrs.	Feels weak and tightness in the chest hours before an attack.	2 brothers and 3 sisters with asthma.	Negative.		Helminthic treatment and vaccines.	No improvement.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
7. M;aet.24 yrs. Labourer.	Influenza.	12 yrs.	Sneezes a lot before an attack.	None.	Negative.	10% (During interval).	Removal of polypi and cure of infection.	Seen 14 months later and there was no recurrence of attacks.
8. M;aet.24 years. Clerk.	Skin disease (urticaria).	24 yrs.	Inclined to be short of breath when sitting quietly and tightness in chest.	Maternal Uncle and Aunt suffered from asthma.	Negative.	10% (During interval).	Attention to bowels, and diuretics.	In 10 days all signs of urticaria and asthma disappeared
9. F;aet.17 years. Labourer.	Not stated.	5 yrs.	Drowsiness and yawning.	Mother suffers from asthma.	Fish and Milk +	6% (During attack)	Vaccine and hygienic measures.	Slight improvement after 6 months.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
10. M;aet.7 years. Schoolboy.	Not known.	2 yrs.	Headache.	Paternal Uncle had asthma.	Not done.		Tab. ephedrine and tonics.	Very much improved 6 months later.
11. M;aet.40 years. Labourer.	Pneumonia and pleurisy.	26 yrs.	Malaise and drowsiness.	Mother has asthma. Brother Hay Fever.	Negative.	5% (During interval).	Peptone injections intramuscularly.	No improvement.
12. F;aet.20 years. Housewife.	Pneumonia.	14 yrs.	Sneezing.	Brother had asthma.	Not done.		Drainage of maxillary antrum.	Cured.
13. F;aet.41 years. Housewife.	Not known.	37 yrs.	Flatulence.	2 Sisters asthmatic	Negative.		Milk subcutaneously.	Improvement for some months and then relapsed.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset,	Age at first appearance.	Premonitary Symptoms,	Hereditary History.	Skin Tests.	Blood Eosin-ophilia	Treatment	Remarks,
14. M;aet 11 years. School-boy.	Whooping Cough.	5 yrs.	Very irri-table be-fore an attack.	Sister asthmatic Cousin Insane.	Negative.	4% (During interval of attack.	Vaccine therapy.	Improved Attacks getting less frequent probably because of near approach to puberty.
15. M;aet.26 years. Shop-keeper.	"Cold in chest".	8 yrs.	Depression.	Mother and 2 brothers with asthma.	positive [illegible] to bacterial protein.		Septal resection.	No re-currence of asth-ma for over one year.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
16. M;aet.13 years. Schoolboy.	Not stated.	5 yrs.	Cough, and Sneezing.	Sister and maternal Grandmother asthmatic.	Negative.	7% (During interval).	Tonic and Quinine.	History shows that attacks are diminishing and the last attack occurred six months ago, probably due to the beneficial influence of puberty.
17. M;aet.12 years. Schoolboy.	Measles and Bronchitis.	4 yrs.	Mental excitement.	Paternal Aunt had asthma.	Slight positive to cat and dog hair.		Removal of 4 dogs and 2 cats from home and vaccines.	Improved

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
18. F;aet.12 years. Schoolgirl.	Not known.	2 yrs.	None.	2 Cousins asthmatic.	Not done.	15% (During interval of attack) stools with Ascaris eggs.	Helminthic treatment and various asthma mixtures and then N.A.B. intravenously.	Improved.
19. M;aet.4 years. Nil.	pneumonia.	2 yrs.	Tightness in the chest.	Sister has asthma.	Negative.		Ephedrin Quinine and Tonic.	Improved.
20. M;aet.7 years. Schoolboy.	Eczema.	3 yrs.	"Flatulence".	Mother and paternal grandmother suffered from asthma	Pork and beans +		C.L.O. and Malt, Tuberculin and avoidance of offending food.	Improved.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
21. F;aet.36 years. Labourer.	Bronchitis.	25 yrs.	Polyuria and headache.	Son and daughter asthmatic.	Not done.		Removal of nasal spur and hygienic measures.	No recurrence of asthma during 6 months after treatment.
22. F;aet.40 years. Labourer.	urticaria and pruritus	35 yrs.	Itching of the body.	None	positive to eggs, milk, cat's hair, and horse dandruff.		Elimination of cats. Diuretics.	Cured asthma. Cured urticaria.
23. M;aet.5 years. Schoolboy.	Bronchitis.	3 yrs.	Irritable in manner.	paternal grandfather chronic asthmatic)	Negative.	6% (During the interval of attack).	C.L.O and malt Tab.ephedrine and vaccines.	Improved.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset,	Age at first appearance.	Premonitary Symptoms,	Hereditary History,	Skin Tests.	Blood Eosinophilia	Treatment	Remarks,
24. F;aet.21 years. Clerkess.	"Cold in the Chest".	6 yrs.	Headache and oppression in the chest.	None.	Negative.		Had treatment before and then injections of N.A.B. intravenously and ephedrine.	Fit and well 9 months after. No recurrence of attacks.
25. M;aet.17 years. Farmer.	Pneumonia.	14 yrs.	None.	Paternal Uncle had asthma.	Negative.		Had other forms of treatment before. N.A.B. intravenously.	No recurrence of attacks for 9 months.
26. M;aet.1 year. Nil.	Bronchitis.	½yr.	Tightness in chest.	Maternal grandmother asthmatic.	Negative.		Castor oil and asthmatic mixture.	Improved.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
27. F;aet.35 years. Housewife.	Bronchitis.	35 yrs.	None.	2 sisters suffer from asthma.	Negative.		N.A.B.intravenously.	No recurrence of symptoms during 2 years after treatment.
28. F;aet.39 years. Housewife.	Influenza and Bronchitis.	37 yrs.	Cough and sneezing.	2 Cousins suffered from asthma.	Negative.		Malt, tuberculin, and N.A.B.intravenously.	No recurrence of symptoms during 16 months after treatment.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
29. M;aet.14 years. Butler.	"Cold in the chest"	10 yrs.	Drowsiness and depression.	Father has asthma.	Negative.		C.L.O. and Tonics, and change of residence.	Improved.
30. M;aet.20 years. Diamond seeker.	Bronchitis.	18 yrs.	Headache and oppression in the chest.	Mother asthmatic.	Slight positive to bacterial protein.		N.A.B. intravenously. (Treated before with no benefit).	No recurrence of attacks.
31. M;aet.29 years. Labourer.	Not stated.	20 yrs.	Indigestion and headache.	Sister asthmatic.	Horse Dandruff + + ; Cat + ; dog +.		Elimination.	Cured.
32. M;aet.51 years. Labourer.	Rice Dust from Rice Mill.	40 yrs.	Cough and sneezing.	Maternal Uncle has asthma.	Hen feathers + + + ; Rice + ++ Oats + + ;		Elimination.	Cured.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
33. M;aet.8 years. Schoolboy.	"Cold in the chest".	3 yrs.	Indigestion.	Maternal grandfather had asthma.	Eggs +++		Elimination.	Cured.
34. F;aet.12 years. Schoolgirl.	Not stated.	7 yrs.	Flatulence.	Father had urticaria; paternal uncle asthma.	slight positive to eggs and milk.		Elimination.	Greatly improved
35. F;aet.15 years. Domestic.	Whooping cough.	5 yrs	Headache and malaise.	maternal grandmother had asthma.	G.pig hair		Elimination.	Cured.
36. M;aet.7 years. Schoolboy.	Whooping cough.	3 yrs.	weakness and drowsiness.	None.	Eggs and Milk ++		Elimination, C.L.O. and Vaccines.	Improved.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
37. M;aet.17 years. Mechanic.	Not stated.	10 yrs.	Headache and depression.	Father has asthma.	Positive to rice, peas and beans.		Desensitisation failed; peptone therapy.	Improved.
38. F;aet.36 years. Housewife.	pregnancy.	21 yrs.	Depression.	Maternal grandmother asthmatic. Father died in Mental Hospital. Sister epileptic.	Negative.		Ephedrine and bromides.	Improved.
39. M;aet.41 years. Merchant.	"Cold in chest".	35 yrs.	Cough.	Mother asthmatic and suffers from eczema.	Not done.	8% (During interval of attacks)	Diuretic and Vaccines.	Improved.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
40. M; 58 years. Merchant.	Influenza.	38 years	polyuria & mental depression.	None.	Not done.		polypi removed; diet & tuberculin.	v.m. I
41. F; 29 years. Seamstress.	Not stated.	13 yrs.	Indigestion & Flatulence.	Father & 2 sisters have asthma.	Negative.		Outdoor Exercise (Cycling) & dieting.	v.m. Improved.
42. M; aet. 35 years. Shop-Keeper.	Indigestion	34 yrs.	Indigestion & depression.	None.	Negative.		Attention to nose & diet.	Improved.
43. F; 40yrs. Labourer	Measles & Bronchitis.	5 yrs.		Paternal grand-father died of asthma.	Negative.		Asthmatic Cough Mixture; Vaccines; & N.A.B. injections.	No improvement.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
44. M; 5 yrs. School-boy.	Eczema & Urticaria	4 yrs.	Cough	Father & Sister asthmatics	Positive to cat-hair.		Removal of domestic pet, Ephedrine; diuretics.	made no difference. Improved
45. M; 70 years. Retired Merchant.	Bronchitis	65 yrs.	"Coryza"	Negative	Negative		Vaccine & Ephedrine	Improved
46. F; 34 years. School Teacher.	Not stated.	29 yrs.	Sneezing & Polyuria	Mother Asthmatic	Negative		Arsenic & iron orally & injections of peptone.	No improvement.
47. F; 20 years. School Teacher.	Pneumonia	12 yrs.		1 son asthmatic	Negative		Thyroid	Recovered
48.								

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
48. F;65 yrs. Housewife.	Not stated	57 yrs.	Drowsiness.	Father asthmatic.	Negative.		Evatmine ..... Thyroid	No effect. v. m. i.
49. F;31 yrs. Labourer	Indigestion	20 yrs.	Flatulence.	Negative	Negative		N. A. B. Injections	Improved (Other forms of treatment did not help.
50. M;6 yrs. Schoolboy.	Whooping Cough.	2 yrs.		Mother had asthma.	Negative.		Ephedrine & Dieting	Improved.
51. M;40 yrs. Mechanical Engineer.	Pneumonia.	30 yrs.	Cough & Sneezing.	Sister died of asthma.	Negative.		N.A.B. Injection Vaccine Injection Peptone Injection Milk Injection.	No effect. Died of cardiac failure ultimately.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
52. M;aet 33 years. Shopkeeper.	Bronchitis & malaria.	23 yrs.	Headache & Cough	Sister has asthma.	Negative.		Quin.& tonic &Asthmatic Mixture; N.A.B. injections.	No improvement.
53. F;aet 25 years. Domestic.	Influenza.	20 yrs	Headache & Tightness in the chest.	Sister & Brother asthmatic.	Not done.		Quin. & Asthmatic Mixture & N.A.B.Injections	Improved.
54. M;aet 35 years. Labourer.	Not known.	25 yrs.		Brother asthmatic.	Sensitive to varnish. Clinically.		Change of residence	Cured.
55. M;aet.17 years.	"cold"	6 yrs.	Sneezing & Coughing	Two cousins asthmatic.	Negative		Ephedrine orally & N.A.B.intravenously.	v. m. i
56. F;aet.9¾ years. Schoolgirl.	Pnuemonia.	2½ yrs.	Cough;Oppression in chest &yawning.	Paternal Grand-father & Brother asthma; Maternal uncle hay fever.	Negative	5% (between attacks)	Autogenous Vaccine.	No attacks while in hospital.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
57. F;49 years. Keeps Boarders.	Not known.	28 yrs.	Flatulence.	None.	Negative.	7% (between attacks)	Vaccines. Dieting.	No benefit. helped for a time
58. F;39 years. Housewife.	"cold in the head."	37 yrs.	Oppression in the chest.	None.	Negative.	12% (between attacks).	Ephetonin & Medicine from doctor.	Helped.
59. F;18 years. Typist.	Removal of tonsils & adenoids & frequent colds.	14 yrs.	Malaise, Sneezing, Cough.	Father urticaria; Mother migraine.	Not done.	10% (between attacks)	Hinchman's Asthma Reliever.	Helps.
60. F;28 years. Housewife.	Not known.	25 yrs.	Stuffy chest & oppression in chest.	Father had asthma.	Negative.	5% (between attacks).	No medicine helps.	

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia.	Treatment.	Remarks.
61. F;45 years. Housewife.	"Colds in the chest"	41 yrs.	Malaise, Cough, Stuffy Chest & oppression in chest.	None.	Negative.	9% (during attacks).	Adrenalin injections whenever attack comes on. Other forms of treatment no benefit.	None.
62. F;32 years. Housewife.	Measles.	2½ yrs.	Cough, Oppression in chest, Polyuria.	One daughter has asthma.	Negative	9% (between attacks)	Removal of polypus & resection of nasal septum; several course of vaccine	No benefit. Now uses Ephedrine which helps.
63. F;3½ years Nil.	Bronchitis	2 yrs.	None	Mother has asthma.	Negative	10% (between attacks)	Bottle of medicine from doctor	Helps.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
64. F;52 years. Housewife.	Coryza & Bronchitis.	41 yrs.	Oppression in chest.	Aged Mother suffers from nervousness.	Negative.	12% (between attacks).	Had two courses of vaccine with no benefit. Uses Blosser's cigarettes which help.	None.
65. F;25 years. Housewife.	Bronchitis.	21 yrs.	Cough & Oppression in chest.	Maternal uncle has asthma.	Negative.	6% (between attacks).	Bottle from doctor helps.	None.
66. F;19 years. Clerkess.	Measles.	5 yrs.	Malaise.	Brother has asthma.	Negative.	8% (during attack).	Vaccines & other forms of treatment no benefit. Uses asthma cigarettes regularly.	

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
67. M;aet.48 years. Asphalt Spreader	"cold in the chest."	33 yrs.	None	Father-gout	positive to meat group.	6% (between attacks)	Tobacco Inhalation helps & also bottle from doctor.	None.
68. M;aet.53 years "Small Holder"	"cold in the chest".	53 yrs.	Soreness in throat.	None	Negative	8% during attack 7% between attacks.	T.A.B. Vaccine & Ephedrine	Was getting attacks while in hospital until T.A.B. vaccines were given him intravenously when attacks ceased to recur.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
69. M;aet.25 years. Miner.	"cold in the head"	22 yrs.	Irritation in throat & Cough.	None.	Negative.	6% (between attacks).	Resection of nasal septum & ephedrine	To report again.
70. M;aet.51 years. Electric Engineer.	Bronchitis & Influenza.	43 yrs.	Flatulence.	None.	Negative.	5% (between attacks).	Moving to higher ground, Hinckman's & Potter's powders help.	None
71. M;aet.47 years. Miner.	Bronchitis.	46 yrs.	Cough.	None.	Negative.	12% (between attacks).	Bottle from doctor no help.	None
72. M;aet.14 years Schoolboy.	Bronchitis	1 yr.	Sneezing, Cough, Coryza & oppression in chest.	Brother has eczema. Mother gets frequent colds.	Negative.	10% (during attacks).	Porter's Asthma Cure helps.	

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
73. M;aet.34 years. Draper.	"Colds in the head".	33 yrs.	"Cold".	None.	Negative.	5% (Between attacks).	Ephedrine helps.	
74. M;aet 20 years. Engineer.	Bronchitis.	14 yrs.	None.	None.	Not done.	10% Between attacks.	Ephedrine and Belladonna help.	
75. M;aet.18 years. Engineer.	Measles and Bronchitis.	6 yrs.	Cough, Stuffy chest, Oppresion in chest.	Father subject to frequent colds.	Negative.	9% Between attacks.	Asthma Powders and Bottle from his Doctor helps.	
76. M;aet.11 years. Schoolboy.	Indigestion.	3 mths.	Yawning, Cold, Coryza, Sneezing, Stuffy chest, Oppression in the chest, polyuria, itching of arms and leg.	Paternal grandmother had rheumatic fever.	Positive to milk and cheese.		A course of vaccine in 1924 did no good, ephedrine helps.	

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks.
77. M;aet.54 years. Shipwright.	Not known.	53 yrs.	Cough, Stuffy chest, Oppression in chest.	None	Negative.		Bottle from Doctor & Hair's Asthma Cure help.	
78. M;aet.14 years. Schoolboy.	Pneumonia.	2 yrs.	None	Mother- Hay fever; Father- Rheumatism.	Negative.		Aspirin, Change of residence, Potter's Asthma Cure, all help.	
79. P.52. F;aet.26 yrs. Housewife.	"Cold".	25 yrs.	Not stated.	None.	Negative.		Attention to bowels; rest.	Slight Improvement.
80. L.175. F;aet.74 yrs. Landlady.	Bronchitis.	70 yrs.	Not stated.	Father- epileptic; Mother- Tuberculosis.	Not done.		Rest, diet, attention to bowel, cough mixture.	Slight Improvement.
81. J.41. F;aet.48 years. Housewife.	Cough	20 yrs.	Not stated	None	Not done.		Diet, and attention to bowels.	V.M.I.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks. On discharge.
82. F.201. F;aet.60 years. Housewife.	Not Stated.	48 yrs.	Not Stated.	None.	Not done.		Rest, attention to bowels; Tr. Lobelia and ephedrine.	Improved.
83. C.161. F;aet.35 years. Housewife.	Not Stated.	35 yrs.	Not Stated.	Maternal Uncle and Cousin on Father's side asthmatic.	Not done.		Rest, Light diet, and attention to bowels.	V.M.I.
84. B.227. F;aet.30 years. Housewife.	Not Stated.	25 yrs.	Not Stated.	None.	Not done.		Rest, Light diet, and attention to bowels.	

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks, On discharge.
85. D.200. F;aet.25 years. Housewife.	Not Stated.	20 yrs.	Not Stated.	Mother - Cancer of abdomen; Father - Cancer of Leg.	Not done.		Rest, Light diet, and attention to bowel.	Improved.
86. A.77. F;aet.42 years. Housewife.	"Cold"	18 yrs.	Sneezing.	Cousin suffered from asthma.	Not done.		Adrenalin, Amyl, Nitrite, Liq. Arsen. and Sodium Iodide.	Much improved.
87. S.207. F;aet.56 years. Housewife.	Bronchitis, and Childbirth.	54 yrs.	Not Stated.	Mother - insanity after childbirth; Father - Senile decay.	Not done.		Rest, diet, attention to bowels. A course of vaccine from stools gave no relief.	V.M.I.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks. On discharge.
88. S.273. F;aet.40 years. Domestic.	Not known.	38 yrs.	Not Stated.	None.	Not done.		Rest, diet, attention to bowels.	No attacks while in hospital
89. T.22. F;aet.42 years. Housewife.	"Chill".	39 yrs.	Not Stated.	None.	Negative.		Rest, diet, attention to bowels, and Potassium Iodide.	Greatly improved.
90. T.95. F;aet.53 years. Housewife.	Influenza.	22 yrs.	Not Stated.	None.	Not done.		Removal of Polypi. Rest, diet, and attention to bowels.	Slight improvement.
91. W.182. F;aet.42 years. Housewife.	Not Stated.	36 yrs.	Cough.	None.	Not done.		Rest, diet, and attention to bowels.	No attack while in hospital

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks. On discharge.
92. H.131. M;aet.14 years. Schoolboy.	Not Stated.	12 yrs.	Not Stated.	None.	Not done.		Not Stated.	
93. R.138. M;aet.32 years. Miner.	Not Stated.	5 yrs.	Not Stated.	None.	Not done.		Vaccine, diet, and attention to bowel.	Improved.
94. R.105. M;aet.47 years. House-painter.	Influenza.	45 yrs.	Not Stated.	None.	Not done.		Pulv: Stramonium peptone (Armour's No.2) intramuscularly.	V.M.I.
95. R.176. M;aet.29 years. Barter Foreman. R.I.E.	Not Stated.	28 yrs.	Not Stated.	None.	Not done.		Attention to bowels, and vaccine made from stools.	V.M.I.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks. On discharge.
96. R.146. M;aet.51 years. Miner.	"Bronchitis".	45 yrs.	Indigestion.	None.	Not done.		Rest, attention to bowels, and vaccines.	V.M.I.
97. Mc.367. M;aet.65 years. Iron Turner.	Thrombosis, and Bronchitis.	62 yrs.	Not Stated.	None.	Not done.		Rest, diet, and attention to bowels.	V.M.I.
98. P.63. M;aet.60 years. Plumber.	Bronchitis.	30 yrs.	Not Stated.	Mother died of Bronchitis, Father died of congestion of the lungs.	Not done.		Rest, diet, and attention to bowels.	V.M.I.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks. On discharge.
99. L.122. M;aet.20 years. Warehouse Man.	Bronchitis.	5 yrs.	Oppression in chest.	Father - Chronic asthmatic.	Not done.		Rest, diet, and attention to bowels.	Much improved.
100. T.17. M;aet.14 years. Schoolboy.	Not known.	Yrs. not known.	Not Stated.	Uncle and several cousins had asthma.	Not done.		Rest, C.L.O. and Malt, Pot. Iodide, and Remedial exercises. (Thyroid ext. did not help.)	Improved.
101. T.11. M;aet.51 years. Painter.	Not known.	21 yrs.	None.	Mother - Rheumatic.	Not done.		Rest, Minimum carbohydrates; attention to bowels.	Improved.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks. On discharge.
102. T.51. M;aet.13 years. Schoolboy.	Not known.	13 yrs. (since birth).	None.	Father has asthma.	Negative.		Tonsils and Adenoids removed. Rest, diet, and attention to bowels.	Improved.
103. T.84. M;aet.18 years. Not Stated.	Not Stated.	Not Stated.	Not Stated.	Not Stated.	Not done.		Not Stated.	
104. H.188. M;aet.34 years. Steel Worker.	Not Stated.	34 yrs.	Not Stated.	Father asthmatic.	Sensitive to cheese, Clinically.		Rest, diet, and Tr. Card.co.	V.M.I.
105. F.15. M;aet.53 years. Miner.	Not Stated.	51 yrs.	Not Stated.	Father died of diabetes.	Not done.		Rest, Cough mixture, and vaccines.	Improved

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks. On discharge.
106. F.184. M;aet.18 years. Not Stated.	"Cold" Bronchitis.	18 yrs.	Sneezing.	None.			Rest, diet, attention to bowel, Ammon. Acet.	Improved.
107. E.6. M;aet.5 years. Schoolboy.	"Bad Cold"	5 yrs.	Cough	Mother has chest troubles.	Not done.		Rest, diet, attention to bowels. Tr. Camph.Co	Improved.
108. A.57. M;aet.49 years. Clerk.	Not known.	47 yrs.	Indigestion.	None.	Negative.		Rest, diet, and peptone intramuscularly.	V.M.I.
109. A.31. M;aet.56 years. Labourer.	Accident.	56 yrs.	Not Stated.	None.	Not done.		Rest, diet, attention to bowels, vaccine from Sputum.	Benefited for 6 mths. then recurred.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks. On discharge.
110. C.223. M;aet.66 years. Teacher of Music.	Urticaria.	64 yrs.	Not Stated.	Mother - epileptic.	Not done.		Rest, diet, adrenalin and boro-calamine Lotion.	Much Improved.
111. C.221. M;aet.32 years. Rubber Worker.	Not Stated.	Since childhood.	Not Stated.	None.	Not done.		Rest, diet, adrenalin, extraction of septic teeth and douching of nose for obstruction.	Greatly Improved.
112. A.101. M;aet.42 years. Shale miner.	Injury.	41 yrs.	Not Stated.	None.	Not done.		Rest, diet, and attention to bowels.	Improved.

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks. On discharge.
113. D.191. M;aet.36 years. Ship Steward.	Not Stated.	21 yrs.	Sneezing.	Mother had asthma.	Not done.		Diet, attention to bowels, calcium lactate, pot. Iodide and arsenic.	I.S.Q.
114. D.221. M;aet.30 years. Barman.	Gastric catarrh.	Since a boy.	Indigestion.	None.	Negative.		Rest, diet, and attention to bowel, and ephedrine.	Improved
115. A.101. M;aet.13 years. Schoolboy.	Cough.	4 yrs.	Not Stated.	None.	Not done.		Rest, diet, attention to bowels; C.L.O. and Malt.	Improved
116. B.260. M;aet.28 years. Farmer.	"Cold"	28 yrs.	Not Stated.	None.	Not done.		Diet with minimum of starchy food. Tr.Lobelia and Pot. Iodide.	Improved

TABULATED CASES.

Number Sex. Age. Occupation.	Assigned cause of onset.	Age at first appearance.	Premonitary Symptoms.	Hereditary History.	Skin Tests.	Blood Eosinophilia	Treatment	Remarks. On discharge.
117. S.265. M;aet.10 years. Schoolboy.	Pneumonia.	3 yrs.	Malaise.	Mother and Brother - weak chest; one sister - Goitre.	Not done.		Rest, nourishing diet and attention to bowels.	Improved.

Letters and numbers in red in the first column of these tables refer to number of the case history.

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