ASTHMA AND THE ALLERGIC SYNDROME.

Thesis submitted for the

M. D. Glasgow

by

William Dick Allan.

M.B.Ch.B. 1916.

Introduction.

For many years past, much research has been carried on all over the world, towards the correlation of asthma, hay-fever, urticaria, eczema, angioneurotic oedema, and other little understood phenomena in specially "sensitive subjects". Freeman (1), has termed these reactions the "Toxic Idiopathies", in an effort to evolve a nomenclature, sufficiently comprehensive to cover every manifestation of sensibility.

New clinical, biochemical, physiological and pathological opinions, are constantly being expressed by the many research workers, who are attempting to investigate this group of phenomena; until the collection of literature on the subject is truly bewildering, and the elucidation of one problem, leads one on to another of more profound complexity.

Bibliographies have been published by Gideon Wells and others, of names allied with this problem, which gives one an idea of the immense amount of work that is being carried on.

One must, I think admit, that the solution of the problem is not yet clear, and from the nature of the processes at work, and the complexity of the factors involved, it is doubtful if allergy will ever be the open book, so many workers of great clinical and scientific attainment have striven, and are still striving, to make it.

Still, by our improved knowledge and methods of treatment, a considerable amount of suffering is being saved today, and if we can even mitigate the attacks, part at least of our mission, will certainly have been accomplished.

Recognising, that if the research of one worker was to be of use to another, some standard terminology was desirable; Kolmer, suggested the word "allergy". Other suggestions have been made by various authorities, e.g., "Toxic idiopathies", "Idiosyncrasy", "Atopy", "Anaphylaxis", etc., etc., but only add to the already too many complications of the subject, by over-burdening the terminology with weighty titles. The symmetrical term to "Aller-

gy is "Allergen", and these terms I will make use of here.

Some reference to the workers of the past seems only courteous, as much was appreciated by them, e.g., Blakeley (2), more than 50 years ago was working out pollen statistics, and these have been repeated and much discussed in recent years.

Hyde Salter, first discovered the dermal reaction, and gave the first description of the "cat poison" - the first wheal, with which Lewis and Krogh (3) are engrossed today.

It is therefore seen what a debt of gratitude we owe to those "pioneers" in allergic research.

Etiological Considerations.

(1) Heredity. Statistics on this point are rather useless, possibly owing to the fact, that no standard of established hereditary laws has been defined, in the investigation of the allergic syndrome, and the different observers have probably been considering one, or at most a few, of the symptoms constituting this syndrome.

Thus, Adam (4) gives his findings as 20%, while other observers give different figures, until Kahn makes the sweeping statement, that the genesis of Asthma lies in the phenomenon of heredity, the conditions being rooted in the biological and physico-chemical structure of the chromasomes, and that 100% of allergy is therefore hereditary; and that until we alter the chromosomal constitution, either in the adult or genetic cells, no cure is possible. This statement is analogous to the oft repeated truism, that one cannot choose one's own grandparents.

Some observers are of the opinion, that asthma is familial, and that definite fixed types of allergy,

persist amongst closely related people, and that asthma produces asthma, urticaria produces urticaria, etc., etc.

This is of course to be expected; homologous strains easily inheriting similar characteristics. Adam, calls this "the inherited bio-chemical outfit".

Personally, I have found in my own cases the percentage to be as high as 90%.

Statistics regarding heredity, would seem also to be upset by the fact, that there may be many persons born with the "hereditary weakness", but in such environment, that no untoward circumstance may occur to cause this weakness to become manifest; and thus they may remain free for years, or may only show some very slight variation from the normal, too slight to be noted.

Tersely it may be said, that the person may be born with the powder ready, but the fuse unlit.

Other observers are of the opinion, that while the allergic state is definitely hereditary, the manifestations may vary. A father may be asthmatic

and eczematous, and the child urticarial and gastric.

My own observations agree with this view, as I have repeatedly seen this occur. For example, I lately saw a child of 6 years with angio neurotic oedema. The father of this child was an asthmatic of the dry-skinned type. When 10 days old, this child had infantile eczema. At the age of 6 months, she developed asthma.

If a child is born sensitised, it has had early intra-uterine and prenatal conflicts with the allergic invader.

It has been shown, that protein may pass through the placenta, and that over-indulgence in particular foods during gestation, might be a causative factor in subsequent food allergy in the child.

Ratner, is of opinion, that the allergen must be a protein, and neither an amino-acid nor a polypeptide. It is not necessary for the protein particle to be reduced to amino-acids before it reaches the blood, and the essential in the mother is circulatory protein, which passes through the placenta, and thus reaches the foetus by this devious route.

Hence early sensitization of the child.

This would explain infantile eczema, which so often attacks a child in the very early days of life. A child may of course, be born sensitized, and may live for some time free from any symptoms, i.e., until the "fuse" is relit by its peculiar "match".

However controversial these conclusions may be, it does seem reasonable to suppose, that the "allergy" lies in the protoplasmic cell, and that the colloids of the allergic individual are not in normal equilibrium; this imbalance being due to his inheritance.

(2) The Nasal Factor.

It is generally recognised, that abnormalities in the nose, play an important role in allergy. The nose is recognised as a "trigger area", which may fire the shot, and start the symptoms.

Hay-fever, at once suggests itself as a nasal manifestation, but in addition, and quite apart from hay fever, it has been shown by the classical experiments of Brodie and Dixon (5), that there is on the posterior and upper portion of the nasal mucous mem-

brane, a definite area which when electrically stimulated, gives rise to broncho-spasm. It is therefore necessary, that the nose must be thoroughly investigated in the study of an allergic case, especially if asthma be present.

Head-colds, sinusitis, spurs and deflections of nasal septum interfering with nasal drainage, are some of the abnormalities frequently associated with asthma.

In asthma, it is very necessary that mouth breathing should cease, if a cure is to be affected, so that the value of a healthy nasal mucous membrane is evident. Adam (6), particularly stresses this point.

The nasal functions are very important, and cannot be interfered with without serious risk of the air losing its filtration and warmth, the olfactory protection being lost, or the ciliated cell action becoming impaired, through loss or local injury to the mucous membrane.

The turbinals themselves, are full of holes and

corners, which form ideal breeding grounds for bacteria, and the numerous accessory sinuses, may function as veritable store houses of sepsis. Taking all these facts into consideration, it is evident, that the nose may form fertile ground for the allergic seed. Some authorities state, that the ethmoidal area is deficient in all asthmatics, and have termed it the "asthmogenic zone" of the nose. Adam, states that 68% of his cases of asthma had nasal abnormalities. Certainly it is evident that any cause, tending to irritate the "asthmogenic zone" must be removed.

Francis (7), who is of the opinion that asthma is due to vaso-motor instability, is also of the opinion that the more normal a nose appears, the more hopeful is the prognosis after nasal cauterisation. He does not agree with the view that the sensitive areas of the nasal mucous membrane, send reflexes through the fifth nerve to the vagus, as stated by Brodie and Dixon, but holds the opinion that vaso-motor stability is the essential, and that cauterisation of any mucous membrane will do.

Whatever view one may support, it does seem

obvious, that disease of the nasal passages, resulting in loss of the protectivity of the nasal mucous membrane, and going on to sepsis, or other complications, will cause an impairment of the filtration apparatus of the respiratory tract. The result of this being, that allergens get right into the alveoli of the lungs, with the possibility of asthma resulting. In addition to this, the toxaemia resulting from foci of nasal infection, may act by keeping the soil sensitive to the foreign proteins.

One cannot help noticing the diversity of results following nasal operations; some cases responding rapidly, while others do not respond at all. I have noted that the asthmatics with the dry, scaly skin, do not respond at all well to nasal treatment, even in the presence of some obvious defect.

(3) The Influence of Trauma.

Trauma may play a role in precipitating what has been called "The Balanced Allergic State"; as although an allergic subject may be apparently quite

fit, it may only require the slightest "push" to overbalance him, and set in motion the complex activities of allergy. The circulatory allergen, will select the weak points in the body, and there the reactions will be staged. Whooping-cough, pneumonia, and bronchitis, often seem to be the exciting causes of asthma. Freeman, is of the opinion that the post-war asthmatic, can date his sensitivity to the damage to the lung epithelium caused by being gassed.

Epilepsy may date from a trivial fall, rheumatism affects the joints and valves weakened by previous injury or disease. Indiscriminate dietary may by chemical and mechanical irritation of a "sensitive" intestinal mucosa, precipitate allergy.

It is well known, that the very slightest pressure can produce a wheal on the dermographic subject.

It is thus apparent, that trauma may be an exciting cause of allergic manifestations, by producing a weak spot, which is pounced on by the circulatory allergens.

4. Other Predisposing Causes.

a. Hepatic function defect.

Recent work has proved that the liver is of supreme importance in the metabolism, and it bears the brunt of the work of protein regulation. It is a highly organised clearing house, and carries out most complicated functions.

It therefore seems apparent, that the allergic states will be precipitated by any hereditary, or functional hepatic defects.

b. Vagotonia.

Dr. A.F.Hurst (8), has constructed an exceedingly pleasing definition of asthma, pleasing, because on first considering it, the problem seems just about solved.

He would have us regard it as, "the reaction of the over-excitable broncho-motor portion of the vagus nucleus, to blood borne irritants, or to peripheral or psychical stimulants". The patient is therefore sensitive to stimuli, which would have no effect on the normal person.

Vagotonia is a nervous condition, characterised by broncho-spasm, slow pulse, contracted pupils, sallow skin, eosinophilia, constipation and hyper-acidity.

It is an indication of autonomic positivity, the sympathetic elements being in submission, the balance of action being in favour of the vagus.

The vagus is however, not uniformly affected, and consequently the symptoms vary.

The occurrence of asthma-like reactions, is to be expected in such vagotonic subjects.

c. The Endocrine Glands.

The functional activity of the autonomic nervous system, is closely associated with the endocrine glands.

Stimulation of the sympathetic will cause increased secretion of the thyroids, pituitary, and suprarenals, and the reverse result will be obtained by stimulation of the para-sympathetic.

Partly owing to our ignorance of their mysterious properties, and partly to our ignorance of the

true mechanism of allergy, it is most difficult to place the ductless glands in their proper niche; difficult to say whether the signs of imbalance of the delicate adjustment and sympathy existing between these glands, is causative of the asthma, or caused by the allergic state. Certain it however is, that in some, if not all cases of asthma, there is marked disturbance of that very delicate and necessary endocrine balance. (I have noted cases showing this fact clearly). (*Vide* cases quoted later.)

d. Visceral defects.

Displacements of internal organs etc., e.g., gastro-ptosis, enteroptosis, ovarian cysts, fibroids, uterine displacements etc., may predispose to allergy. Hurst, mentions that distension of the stomach or rectum, may reflexly cause the start of an attack owing to pressure.

e. Habitus - Idiosyncrasy.

It is sometimes said, that a small section of sufferers, are apparently, asthmatics and allergics

by habit and peculiarity, but I am of the opinion, that psychological factors per se, are not causative. A strong emotional stimulus however, may induce an attack in a highly responsive subject.

The Channels of Entry.

The skin and the mucous membrane, are the two chief sites for the entry of allergens. The skin is well known for its absorbent properties, and the mucous membranes of the respiratory and alimentary systems, offer a huge surface for the reception of foreign proteins. The reaction does not necessarily take place at the site of entry, as although the signs are local in hay-fever, it may also be produced by alimentary ingestion.

The Exciting Causes in the Allergic Syndrome.

Having considered the soil upon which the reaction takes place, and also the sowing of the seed, it now seems opportune to consider the types and peculiarities of that seed, and to study its growth and development, towards the harvest with its complex

reactions.

There is still much controversy with regard to the direct,and to the exciting causes in allergy. Some are of the opinion, that it is a sensitization phenomena pure and simple, (closely akin to anaphylaxis) the subject being sensitive to a particular protein, which sensitivity is developed by a primary sensitizing dose, and excited by further exposure to that particular protein or allergen, be it pollen, food protein,or dust.

Intestinal toxaemia, the result of deficient protein digestion, in the presence of excess of carbohydrate, is considered by others to be the source of the trouble.

Amongst those who uphold this view are Adam,(9) Haseltine and La Forge (10).

In Holland, Van Leeuven (11) working in a low lying country, considers the dusts and moulds as causative factors.

Another section of authorities, influenced by the physics and chemistry of the colloids, are of

opinion that the real cause must be looked for there. Willcox (12) and his followers, have used that most comprehensive, but vague term "occult sepsis", to cover the etiological solution.

Pollen, animal emanations, emotion, idiosyncrasy, climate, infections etc., etc., all have their partisans. The allergic reaction is so complex and comprehensive however, that various as are the views held, all are probably in some degree right.

The reaction may be, and probably is, the result of several of these causes acting at the same time, but in considering allergic phenomena, we must also always consider the "protein-poison".

1. Cutaneous testing for specific proteins.

Observers in America, as well as Latham & Coke (13) in Britain, have carried on work on the causation of asthma, and I think most of us were much impressed by their findings. They claimed, that by testing the skin for various proteins, by rubbing in an extract of each, and by observing which produced "whealing", (The Arthur Phenomenon) a definite diag-

nosis could be established, and after that, all that was necessary, was to diet,or to desensitise the patient against that particular protein. This seemed quick, definite, and concrete; and was also impressive to the patient. Most of us I think, have found that this method has not come up to our expectations, mainly I think due to the impossibility of absolutely standardising the technique etc.

2. Food and Allergy.

Many foods prove to be causative factors of asthma, and the other allergic disorders; due to the fact that they contain complex proteins, which do not pass through the normal routine in their digestion. Such defects are liable to occur with any protein. Sometimes it is a question, not of the protein itself, but of the end-product.

There is no doubt however, that undigested protein is a cause of asthma, more especially in conditions where we are dealing with hepatic deficiency, and intestinal abnormality.

It has been demonstrated that under certain conditions, there was the absorption of undigested protein through the villi of the intestines. Hartridge (14), states that proteins have been discovered in the cells of the villi, and he concludes that they have been synthetised, although he also points out that eripsin may act on any incompletely hydrolised protein which has got into the epithelium of the villi and reduce it there, to its particular amino-acids.

There is thus normally a two fold action, and it is possible that sensitivity may prevent these reactions in an allergic subject.

In allergic subjects therefore, the proteins would seem to be allowed through the epithelium, in a much more highly organised state, than in the normal subject.

This explains many of the resultant symptoms which are encountered.

Hansen (15), is of the opinion that the whole question of food sensitivity is solved by the proof

of the principal, that it only requires a temporary damage of the mucosa of the intestine, as in enteritis, to permit of absorption of the imperfectly dissolved protein molecules; a further proof that the seed may develop on the prepared soil. The above evidence proves the occurrence of protein transference from the bowel to the blood.

(3) The Part played by Toxins.

It has frequently been stated by authorities, that the allergic syndrome is a toxaemia, and probably most frequently an intestinal toxaemia.

The hypothesis that, "if asthma is caused by intestinal toxaemia, a definite toxin exists, causing bronchial spasm, similar to the effect produced by muscarin, and that this toxin must exist in the intestinal canal", naturally arose.

It was then demonstrated, that putrefactive action on amino acids, caused a liberation of CO_2 and "amins" were formed, including "histamine", which "amine" causes the broncho-constrictor action etc. (Dale. 16). Eustis, isolated this base from the

faeces of asthmatics, but could not demonstrate it in the blood. He therefore concluded that there was a strong possibility of allergy being caused by this toxin being present in the bowel.

Adam (17), holds that the toxaemia arises partly in the tissues, and partly in the bowel, and admits that the poison may be the result of microbic action. His chief principle however, is, that the error is one of nitrogenous metabolism. The error he states, arises from protein food and protein tissue, and together with this is carbohydrate excess.

The digestion of the carbohydrate molecule, appears to "starve" the protein of its proper enzymes and the result is protein-poisoning.

The foci of bacteria producing the toxaemia, obviously however, may be in the naso-pharynx, bladder, kidney, uterus etc., etc.

4. Bacteria. Streptococci of various strains have been demonstrated in the throat, in the faeces, and in the duodenum of patients suffering from asthma and angio-neurotic oedema.

Varieties of organisms are also frequently found in the sputums of asthmatic subjects. It therefore does seem reasonable to utilise vaccines in the treatment of asthma, with the assurance that their exhibition will probably meet with some measure of success.

(5) Pollen.

Pollen chiefly in the form of Timothy grass, is, during the summer months, chiefly responsible for hay-fever in this country. It is clearly demonstrated, that the sharp nature of the pollen granules makes them very formidable as irritant factors for the nasal mucosa.

Pollen can, however, produce other allergic manifestations besides hay-fever, and its symptoms from a central focus, are simply different from those of a peripheral focus.

(6) The Role of Dandruff in Allergy.

As dandruff is epithelial scaling, it is evident that in the atmosphere of a city, we must be in contact with the scales of horses, cats, dogs,

humans and other animals.

The susceptibility of certain people towards the emanations of cats, dogs and horses, is well known.

In the investigation of allergy, we must therefore take stock of the domestic pets, etc., and exclude them if necessary. The problem is made more complex, from the fact that in our civilised life, we are all breathing a mixed atmosphere, and therefore, those of us who are sensitive to animal dandruff will at once, show evidence of allergic symptoms.

To treat those subjects satisfactorily, isolation in pure, un-contaminated air would be necessary - a very difficult treatment to follow.

(7) Dust and Allergy.

Modern dust in cities and closely populated areas, contains shreds of all types of protein, including pollen, dandruff, molds, bacteria, and other protein forms.

Van Leeuven (18), who is a great authority on the dust-factor in allergy, has conducted most

interesting and instructive experiments with dust-proof chambers.

The chamber is supplied with filtered dust-free air, and the patient is living in a completely dust-free atmosphere. The results of this treatment have been most encouraging, and it is found that patients are much improved even by sleeping in bed-rooms, equipped with filter-apparatus.

Van Leeuven, has also carried out much work on "Climate allergens", or "miasms", and he finds that 90% of his patients are relieved after three days at Davos.

This he considers to be due to the absence of "miasms". However, the altered oxygen content of the air at that altitude, and the physical effect of the air pressure at Davos, may I think, play an important part in the relief of these cases. It is very difficult to generalise about the effect of changes of climate. For example, I have a patient, who suffers violently from hay-fever during June and July in Scotland, and who time and again has been immediately

relieved on going to Blackpool, a town at sea level. Neither is it the sea-air, as going to other sea-coast places, has not the same effect. It is apparent that the effect of dust with relation to allergy is not an inconsiderable one.

(8) Miscellaneous Exciting Factors.

Serum rashes are allergic phenomena, and are probably due to the contained proteins, and drug rashes are probably of much the same nature. Viruses, inter-creations, and infections, all depend on incompatibility of the body protoplasm with the particular agent.

Emanations, mechanical, physical and psychical factors, ought it would seem, to be grouped together, as stimuli which act obscurely and about which much is still to be learned.

Parasites, such as mematodes, throat worms, have been shown to produce severe allergic reactions.

Some authorities state that the convulsions in children associated with throat worms, are allergic manifestations.

The Pathology of the Allergic Reaction.

In allergy it can be concluded that the "seed" represented by the various allergens already discussed, acting on the highly sensitive "soil", through the skin or mucous membranes, produces a definite type of reaction, which varies with the area involved.

This reaction, which is of a definite type, may take the form of exudation, catarrh, spasm of muscle, blood changes, changes in the cells, or reaction of an anaphylactoid nature. The pathology of the last named (being of a temporary nature) cannot be discussed, as it is a phenomenon of physiological chemistry, which does not show histological changes. However, the spasm of muscle, exudation and catarrh of the tissues, also the blood and cell changes, can be demonstrated by microscopic means.

1. Gross Pathology.

The gross pathological damage is not as a rule very great.

Naked eye examination of organs, unless in very long standing, and complicated cases, revealing only

slight alterations from the normal. It depends upon the site of the reaction, whether we have a lesion of the skin, of the lung, or of the mucous membrane, but it may be stated, that wherever the fine chemical and physical changes take place, there is produced an exudation of fluid, and a catarrh of certain cells. The blood, which is the vehicle conveying the excitant to the tissues, shows definite changes in the eosinophile cells, while the reaction in the lungs is myoplastic in character. This has been demonstrated by Dale (19).

Generally speaking, the reaction to the irritant may therefore be said to take place where capillaries exist, and a constant result is catarrh, exudation, cellular changes and blood and muscle peculiarities.

With the above pathological changes in progress, symptoms are produced according to the degree of involvement of the tissue affected, and thus in the skin we get urticaria, eczema, pruritis, and other forms of dermatitis; while in the deeper layers we

get an actual oedema.

In the lungs we get exudation, catarrh, and myospasm, while in the nose we have catarrh and exudation. In the alimentary system, there is a preliminary exudation, followed by catarrh of the mucous membrane and hepatic ducts. This may lead to chronic conditions producing vomiting, diarrhoea, and mucous-colitis. Migraine, convulsions, and epilepsy, may be reflex cerebral symptoms - the result of toxaemia, or they may really be the results of reactions which are being staged at the site of capillary change.

The paroxysmal swelling of joints can be explained by a similar condition of the synovial membranes, and there are some authorities who would fain include acute rheumatism, as yet another symptom of the allergic syndrome.

Adam, mentions the occurrence of paroxysmal albuminuria, and renal asthma is already recognised.

Paroxysmal haemoglobinuria may result from the least change of temperature, and it may also be an allergic reaction.

Eosinophile.

This is one of the most constantly found conditions in allergy, and if proof were required to connect the various manifestations of the allergic syndrome, eosinophile would about supply the evidence.

Adam (20), made a most interesting contribution to this question when he stated, that the greater the allergy, the greater the eosinophilia.

It was in the nature of an index, the sputum being always full of eosinophiles, when the CO_2 was trapped by broncho-spasm.

The eosinophilia may possibly indicate some blood response to acidosis, which undoubtedly exists in allergy.

The full biological significance of eosinophilia, has yet to be demonstrated, but we may accept it meantime, as a valuable sign of the reaction of haemopietic tissues to the protein poisoning.

The Anatomy of the Capillary Vessels.

Owing to the nature of allergic reactions, it is evident that the capillary vessels play an important part, and much study is being directed to them.

It has been demonstrated, that the capillary is not merely an endothelial tube of a passive nature, and of variable size, but that there is a fine reticular muscular coat proceeding from the "Rouget-cells," which are presumably the representatives of the muscle cells of the arterioles. In the capillaries, the muscle elements are reduced to a minimum, the wide mesh network allowing for the passage of substances with the least trouble, which passage would be impossible in a three coated arteriole. These cells have a definite tonus ~~aperture~~ or posture, and are capable of flattening out, when required to raise or lower the tonus of the capillaries.

In the liver, Rouget- cells are not present, but there is a type of adventitious layer present, probably enclosing a lymph space, and the capillaries in this organ are more permeable to dissolved sub-

stances of a colloid nature, than those in other organs.

The innervation of the capillaries, and whether they are subject to sympathetic impulses etc., is still not clear.

The Importance of H substance.

Histamine occupies an unique position in the physiology and bio-chemistry of the allergic reactions.

Histamine or ergamine, is produced when the amino-acid histidine loses its CO_2 and it is always found, when protein is broken down in the presence of putrefactive organisms. It is therefore common in meats, the intestines etc., and has been extracted from the gut, liver and lung etc., and pharmacologically, it is a potent poison. Large quantities of histamine have been, for purposes of experiment, injected into the tissues, and it was found that there was a marked fall of B.P., and that the great veins were found to be lacking in blood. The arterial system was also found to be lacking in blood, but when the capillaries and vessels were investigated,

especially those of the abdominal viscera, the blood was found accumulated there, as in surgical shock.

The term "dilator hormones", has been applied to those H-substances, and although nothing very definite has been established, some authorities consider histamine to be liberated mainly from the lungs; others, that it is a secretion from the tissue cells.

Clinical experience of allergic states, has proved that adrenaline is antagonistic to histamine. Prolonged intestinal putrefaction tends to overstimulate the adrenals, which become exhausted in neutralising the H substances.

Histamine, or at least an H-substance, is undoubtedly the most important derivative active in the body. Its complex functions have not been fully recognised, and we know more of its toxic properties, than we do of its undoubted role in the regulation of the circulation, the control of gas, and food exchange, and the preservation of the metabolic balance. It may be a hormone, or a normal analytic metabolite - which, we at present cannot definitely state.

The Relation of Capillary Action to Allergy.

Capillaries can open and shut as required, by stimuli received from that area they supply, and so an organ or area, can call upon its vessels for a full supply of blood when it is active, and requires it, or it can, when at rest, dispense with the majority, and continue to live with a much reduced supply.

These stimuli may be traumatic, chemical, mechanical or psychical.

Take for example, what occurs when a small area of skin is injured by some agent. There are two distinct types of reaction:-

(a) A local direct and immediate reaction of the capillaries limited to the area stimulated. This is a morbilliform rash, - a typical "wheal".

(b) An area of redness, the "flare" of scarlatiniform type, and the result of dilatation of arterioles, as an effect of local stimulation of terminal branches of nerves. The two conditions taken together, are indeed a true urticaria.

What has happened in the tissues to cause this

exudation, and allergic manifestation? Some authorities say it is histamine, while others disagree, but it does seem reasonable to suppose that by some means H substance has become liberated, and that it acts on the endothelium of the vessels at once; later to spread to the nerve controlled arterioles and cause vaso-dilatation. The H-substance is gradually neutralised, and the reaction passes off; but not until the adrenal and pituitary hormones have, by increasing their secretions, tried to neutralise, or fight the injurious agent.

There has been a great deal of most delicate and exquisitely "baffling" work done on this subject, which with its attendant volumes, adds to the enormous library already existing. The function of capillary exchanges, is a most complex one, as we have involved gases, water, inorganic salts, organic crystalloids, and sometimes even colloids, and it is quite beyond the scope of this memo. to attempt to review the long involved discussions on the osmotic pressures, diffusions and absorptions, associated with it.

It is very difficult to state definitely what is really taking place in amino-acid exchange, between the capillary epithelium and the fixed tissue cells, but it seems fairly definite, that in the disintegration of cells, histamine is set free, and also other more complex colloidal substances, which may have other actions on the minute vessels.

Krogh (21), discusses also the action of acid-metabolites, especially CO_2, which is an index of increased metabolism. There seems no doubt, that venous hyperaemia is brought about by the tissues themselves, reacting to these substances.

The hydrogen ion content of the blood is normally 7.35, and by means of its buffer-substances, and other protective factors, the blood remains constantly at this level. It is admitted, that the pH of all tissues may rise to the region of 7, but there are necessarily very narrow limits, if the equilibrium of the body fluid is to be maintained, and perfusion allowed to occur normally.

Deficient oxygen is also an element in the com-

plication, and may have much to do with the increased supply of blood to the active organs. It is recognised that any acid substances, when brought into contact with the living tissues, brings about a mobilisation by simple diffusion of the hydrogen ion into the tissues, which become reflexly increased in pH. The buffer substances however, become active, and an automatic levelling-up takes place, thereby neutralising almost completely, the effect of the acid on the living tissues.

Summing up of this situation is most difficult, but by certain eminent authorities it is agreed, that the tissue cells by various diverse stimuli, liberate dilators of the smaller blood vessels, but it is controversial whether histamine is a constant, and whether it is a normal metabolite. In various parts of the body its action varies. In damage to the cells of the skin or other organs, histamine, or a substance very like it is liberated, and this acts on the vessels in the manner described. The amount liberated is variable, just as the stimuli are variable, and

it is possible,that allergic reactions such as asthma, urticaria etc., may be due to local capillary selection, or to histamine concentration.

Indicative of this, one finds that the chief sites for allergic manifestations, are at the areas of capillary exchange, i.e., the skin and the lungs.

The Symptoms of Allergy.

It has already been indicated, that allergic reactions take place mainly at the site of capillary exchange. Asthma, urticaria etc., are but symptoms of local disease,and are but the outcome of a metabolic reaction, stamped with the characteristics of its locus. With these facts in mind, we will now attempt to group the symptoms of the syndrome.

1. Anaphylaxis and Allergy.

Much has still to be proved about the peculiar reactivity or reaction - Anaphylaxis.

The relationship between Allergy and Anaphylaxis, has been the subject of much controversy, but one may accept the view that allergy is "anaphylactoid", if not an attenuated variety of anaphylaxis itself. Anaphylaxis is an antigen - antibody reaction, and the development of its peculiar sensitivity can be explained on the lives of Erlich's side-chain theory.

In animals, the reactions of anaphylaxis vary greatly; one may exhibit pulmonary symptoms, and another gastro intestinal. This, in the opinion of some authorities, strengthens the bond between allergy and anaphylaxis, because in allergy there are admittedly different groups of symptoms formerly thought to be distinctive diseases, and the colloid state of protoplasm is intrinsically, the reason for all anaphylactoid activity, varying in its reactions according to the animal.

2. Allergy and Asthma.

Asthma is the most dramatic and distressing symptom of the allergic syndrome, and one of the most urgent problems in medical research today. Asthma is the result of broncho-spasm, caused by a circulatory toxin, and the net result of all the experiments which have been conducted, is that asthma must be regarded as an allergic reaction, dependent upon poisoning of smooth muscle, complicated in chronic cases by bronchitis and emphysema, and the outcome of protein-hydrolysis.

This definition is of course controversial.

3. Allergy and Epilepsy.

It is well known and widely recognised, that a large percentage of cases of epilepsy are hereditary, and it has also been stated by certain authorities, that epilepsy and allergy are closely associated.

There seems no reason why the epileptic seizure should not be of an allergic nature, as the very refined, and finely balanced cerebral cells, seem to lend themselves as a suitable site, for the

staging of an allergic reaction.

(4) Allergy and Eczema-Urticaria.

Urticaria and eczema, are really the same condition, the former being merely an acute form, and histologically the only difference seems to be in the degree of oedema.

It is generally recognised, that eczema and urticaria usually occur early in life, and are frequently the fore-runners of asthma. It is also common to find asthma and eczema in the same patient, or the child of an asthmatic, suffering from infantile eczema. The family history is also strong evidence of the allergic tendency of eczema, while the reactionary tendency of urticaria to food sensitivity is generally recognised.

(5) Allergy and Rheumatism.

That the cause of rheumatism is one of the medical world's "unsolved mysteries" is obvious to all. The microbic theory, at present represented by the organisms of Pointon & Payne, has its ad-

herents, while some authorities suggest, that it is a new type of immunological manifestation which is being uncovered. The joint troubles associated with serum sickness are very similar to those of acute rheumatism, and the joint fluids in both are also sterile.

Paroxysmal hydarthrosis, and certain other conditions, seem analogous to angio-neurotic oedema.

Exposure to damp, cold and microbic infection, predispose to both allergic conditions and rheumatism.

Conclusions.

The established reactions of the allergic syndrome are undoubtedly associated, and it is only a matter of "build" or constitution, which determines the organ affected, and influences the resultant manifestations.

We scratch eczema, or scratch a wheal until we let the toxic fluid out; we vomit and purge when alimentary exudations are present, and so get rid of them; we cough and perform forced expiration, until we expel the thick and tenacious mucus, the result of exudation and catarrh in asthma.

In fact, all our actions are aimed at ridding ourselves of the irritant fluid.

Adam (22), sums up the situation excellently when he says, that in the allergic reaction hydration is at its height or maximum, and is washing out the tissues from within. The whole mechanism of the body is, in this widely toxic condition, employing every effort possible to get rid of the trouble within its walls.

If we regard allergy in this light, the constituents of the syndrome are readily related and reconciled.

McDonagh (23), in summing up the situation says, "hypersensitiveness means no more than augmented hydration, and removing the agent causing the same, does not get rid of the factor which set the original hydration in motion".

This hydration is hereditary, and thus all the constituents of the syndrome are merely manifestations of inherited peculiarity or idiosyncrasy.

The Chemical and Physical Pathology of Allergy.

The biophysics and the bio-chemistry of the condition must be investigated in a discussion of the mechanism of Allergy.

Adam, characterises the reaction as depending on "the inherited biochemical outfit", and sums up the situation by saying that allergy is an acidosis, in which there is a struggle by the blood to retain its normal pH. The condition is thus a toxaemia, characterised by imperfect oxidation and enzyme action.

The basis of a proper understanding of this condition, is a realisation of the fact that the fluids and the cells of the body are composed of colloids. It seems fairly definitely established, that a protein is the causative factor, and all allergens are accepted as being proteins, whether they be of the nature of bacteria, metabolites, or other forms.

Assuming that in the normal course of protein digestion the proteins are hydrolised to globulin, alkali-metaprotein, the proteoses, peptones, polypeptides and finally amino-acids, the vital question is that of the absorption of these acids.

Normally it may be stated that the protein elements of the food enter the blood in the form of amino-acids, being conveyed from there to the capillaries via the liver, the hepatic cells de-aminising the amino acids which are not required for protoplasmic repair, thus acting as an efficient filter. Arriving at the capillaries, a very complex activity occurs, depending upon capillary blood supply, surface tension of the blood, and of the plasma outside, hydrogen ion concentration of all the colloid tissues, osmotic pressures of the various fluids involved, and indeed sufficient chemical and physical activity to provide material for a large volume on colloid chemistry and physics alone.

The Biochemistry of the Allergic Syndrome.

An analysis of the blood, urine and other secretions, is an index of the complex processes involved, and it would seem easier to follow the reaction of allergy from its end-products backwards, so to speak.

In this amino-acidosis, with its reduced

urea, both in the blood and urine, the organism is having a battle to maintain its pH of 7.4. Adam stresses the point that the "chloride-shift" is in operation, the hydro-chloride going to the corpuscles, while sodium is free to unite with the carbonic acid gas; yet another attempt on the part of the blood to deal with its acidosis. McDonagh (24), gives a very helpful summing up when he states, that hydration is the clue to the situation, and points out that histamine bears a powerful positive electric charge, and this explains its potency. Reaction is simply a degree of hydration, and cellular response depends upon the extent of it. He also states, that the expiratory difficulty is not due to broncho-spasm, but to lack of oxygen, and also that the eosinophile granules are destined to disperse the hydrated protein particles.

Hydration is hereditary, and once more Adam's statement re "the inherited biochemical outfit" is borne out. If we accept hypersensitiveness as equivalent to hyper-hydration, we have discovered the

reason for allergy, but as McDonagh points out, it does not get rid of the diathesis.

The relative proportion of calcium and potassium in the blood is a vital factor in the equilibrium between the vagus and sympathetic nerve supplies, but we find that the blood calcium in allergic subjects is fairly constant, 7 - 11 m.g. per 100 c.c., being a common reading.

The chloride content of the blood is low, due to chloride being taken up by the tissues and so retained, chlorides being absent in the secretions during an attack.

With regard to the urine, the ratio of free acid to ammonia is altered, so that a rise of ammonia is common in the urine, and before a paroxysm urates are numerous. After an attack, diuresis takes place, with increased acid in the urine. Adam stated that the polyuria was an attempt to get rid of the acidosis.

Owing to the broncho-spasm there is an excess of CO_2 in the blood, and the acids may unite with calcium. The oxygen given up by the haemoglobin liberates the bases, but in the blood we also have the

"buffer-action" of the Sod. Bicarb. and the sod. phosphate, which keeps the pH constant. The "chloride shift" keeps the blood alkaline. Adam regards eosinophilia as a chemistactic response of the polymorphs to acidosis. The nitrogen is used up by the formation of amino-urea, this becoming ammonia in the kidney, there being an increase of ammonia in the urine, and a decrease of urea.

The part played by the ductless glands in regulating metabolism, is certainly of great importance in allergy.

When it is realised that all the ductless glands are over-stimulated by the toxaemia, in an endeavour to antagonise the H substances, adrenaline fatigue is only natural. The beneficial effects of high altitudes, and the much more easily obtained benefit of cold baths, as recommended by Adam (24), both act by stimulation of the supra-renal bodies, as well as from other causes. The eosinophilia seems also a reaction to increased adrenal function.

Status-asthmaticus means acute adrenal defect,

and can only be counteracted by continuous adrenaline administration as recommended by Hurst (26). Lastly, blood cholesterol has been found increased in asthma, and also urinary diseases, no doubt connected with the increase of eosinophiles, but this branch of biochemistry is still obscure.

To sum up and take stock of all the facts is most difficult, but we may be on the eve of getting a definite set of factors, which will be the indices of the allergic condition. Asthma notoriously begins about 2 a.m., the period of the "acid-tide", and all evidence strengthens the conclusion that the condition is one of true acidosis, and reaction to the hydrolysis which has taken place, and which is still in action all the time the symptoms persist.

The Nature of Allergy.

To co-ordinate and correlate all opinions as to the processes at work in producing the allergic syndrome, is a task never yet accomplished, and no one has evolved a definite set of features which can be found constant.

Some important and definite facts however, stand out which are apparently unassailable.

Allergy is undeniably a toxaemia, and asthma, eczema, urticaria, and other so called diseases, are but late signs of defects in a "biological curio".

Whatever the vital and involved processes at work may be, the slightest change of circumstances, chemical, physical, and emotional, may become uncontrollable stimuli in the production of protoplasmic disintegration.

The spasm of asthma, the group of wheals etc., are all evidences that something fundamental has occurred, and that the body is striving to establish its normal equilibrium; is making a stand against adulteration of its protoplasm.

It is necessary to have a sensitised subject with an inherited predisposition, and colloid particles that are unduly mobile.

The allergic subject may thus go about comfortable and free so long as he does not have the coinciding factors, which together produce the upheaval. If he has tissue damage however, of any description, which reacts to the "trigger" which is pressed, his attack will be precipitated.

It is generally agreed, that the nature of the activities indicate an antigen-antibody reaction, and the cellular theory has become firmly established.

The antigen uses the blood as a vehicle, and no doubt the cell provides the ferment and enzyme against the invader, and in so doing, it may produce antibodies which are errant, but the strongest possibility is, that the antibody is fixed within the cell, and has its activities confined to the cell. One product at least of the antibody reaction is Histamine.

Life is essentially protein, and the most elementary living molecules are polymers of amino acids,

and although we know less than a score of amino-acids their polymers may amount to millions.

A simple unadulterated protein does not exist; a carbohydrate or gluco-group is essential, and sources of varied energy, such as light, heat, electricity or chemical action, acting upon the molecule in its fundamental medicine, activates the "battery"; and so potential energy produces kimetic energy, the rate of discharge of the latter depending upon the irritability of the type of matter. It is evident, that the old doctrine of "omnis cellula ex cellula" has suffered considerable change.

Much work has been conducted by certain authorities who doubt the cell as the unit of protoplasm, and they have demonstrated, that there exists a living corpuscular element, about the same size as a colloidal micella, a parasite, of what we have always regarded as the lowest possible parasite, namely, the bacterium.

It is found in the intestines of animals, in water, in earth, but it needs the bacterium as food.

Much research is of course necessary before we can appreciate this fully, but it will have far reaching effect as regards bacteriology, etc. As bacteria are antigenic, and are facts in the cause of allergy, being indeed glyco-nucleo proteins and complex, it is evident, how much the antigen-antibody reaction of allergy may be influenced by such minute constituents of life.

Thoughts on the colloid nature of protoplasm, and on its exquisitely developed sensitiveness and reactionary power, lead one to consider the chemical and physical reactions of protoplasm, and to regard its functions as dependent on that unknown item, which we may call the "vital-force" or "life", and which is activating all its actions and reactions, making us realise, that neither chemistry, physics, nor any other science, will ever reveal that "life".

There is a different type of protein for every individual, and thus we are all distinct from one another, are "individuals".

Protoplasm being living matter, must live,

so whenever a living cell is brought into contact with a protein, it at once, by enzyme action, acts on, and changes that protein, thus the good food is accepted - the bad rejected.

In all assimilation processes, the continuance of life depends upon the ability of the specific protoplasm to convert heterologous protein into protein homologous with its own composition, and when this process breaks down, the result is poisonous accumulations in the body. Therefore, the more the heterologous protein resembles the tissue with which it is in contact, and the more its amino-acids etc., are in harmony with its host, the more will that protoplasm remain constant in molecular construction, and the more refined will it continue. Vitamines, hormones, and enzymes, are therefore of vital moment.

This constant conflict to maintain protoplasmic purity, is the saving of individuality, and the standardisation of species. The maximum effort of the body corporate is thus demanded, and the allergic syndrome, is but the excretory phase of the tissue

reaction. Treatment of the allergic diseases will therefore be required to aim at something more elusive and complex, than the gross spasm, itch or catarrh.

Some doctrines of treatment of the Allergy Syndrome.

The obscure and complex origin, and the intensity of the symptoms of allergic conditions, has resulted in a most bewildering mass of treatment, so perforce one will only refer to the proved methods, and those which have been evolved from scientific and logical methods of investigation.

Allergy is not in the true sense of the word a disease, but rather an atypical type of individuality.

Drugs etc., may possibly relieve its end-products, its more urgent reactions; the phase of the trouble we are most in contact with. We may blame ourselves for beginning at the wrong end, but as practitioners it is often the only end we see.

And so, we have gone through the phases of atropine, pituitrine, adrenaline, ephedrine;- the feather bed has been banished in favour of the flock mattress - the dog, cat, or canary, have been"given their papers" - the patient has been shut up in dust-proof chambers, - psycho analysis has been dragged in, to exert its very doubtful influence on

the mind of the much maligned "neurotic" - inhalations - antispasmodics etc., etc., have all been tried. Yet with all these, the body carries on the struggle to keep its protoplasm free from taint, and that it has succeeded is proved by the low death rate from pure allergy; and we must give it all the help we can.

It is obvious that if allergy is, as we are supposing, a protein poisoning and an acidosis, all effort must be made towards the removal of the poison, once it has been identified.

Knowing also the hereditary defects of the allergic, methods must be adopted to remedy these defects, and so protect the organism from its environment.

These two principles sum up the essential treatment, if relief is to be obtained with any degree of permanency.

Van Leeuven (27), is a keen advocate of the principle of air filtration and the use of allergen proof chambers, as diagnosis is simplified and desensitisation can easily be carried out. Many

other authorities have given their approval for this treatment.

Adam (28), points out the great difficulty of carrying out biochemical investigations on asthmatics, for as we all have noted, the asthma is inclined to disappear in hospital.

High altitudes, where the atmosphere is purer and freer from moulds, spores etc., is recommended, and the increased oxygen tension at these altitudes may be a considerable help.

Dieting and hygiene are very important, as we are dealing with a diathesis, and certain drugs, e.g., iodine, and in fact anything which will help in the removal of chronic intestinal intoxication will help.

X-ray treatment has, according to some authorities a future.

Gilbert Scott (29), referring to the imbalance between the endocrine glands is of opinion that X-rays keep the ductless glands in harmony. The effect on the polarity and electrical reactions of the various colloid particles, is no doubt also

powerful, possibly altering the relativity and helping to restore harmony. This treatment is however still in its infancy, and whether it will succeed or not, is still to be proved.

Peptone treatment, which for a while held the stage, has to say the least, not come up to expectations.

Vaccine treatment has undoubtedly earned its permanent place in the treatment of allergy, as is only natural in the presence of a source of infection. Morley Agar (30), treats the ears, face and scalp (i.e., the distribution of the fifth nerve) with carbolic acid, peppermint oil and spirit, and states that he obtains excellent results.

Alexander Francis (31), works along similar lines when he cauterises a mucous membrane in an attempt to increase the vaso-motor tone.

Grant (32), and others, stress the importance of treating the sensitive nasal septum, (the asthmogenic area) and rectify other nasal abnormalities.

Clement Francis (33), has stated that the remov-

al of polypi in a person not sensitive to aspirin, will benefit the asthma, and he agrees with Alexander Francis, as to the influence of the vaso-motor centres.

Personally, I have obtained good results in juvenile cases, with the treatment which will be found in my notes on child cases. Of course, it is evident that one cannot draw any conclusions from one's own few cases.

Methods of routine treatment.

Hansen (34), made an excellent suggestion when he stated that for the efficient treatment of a case of asthma, a board of doctors, including a bacteriologist, radiologist, nasal surgeon etc., was necessary. This has now been done by the Asthma Research Council, at least in a limited manner.

The main routine principles I think are:-

1. A decision as to the probable allergen.
2. A summing up of the patient's "biochemical outfit".
3. A careful watch for occult sepsis.

4. Vaccines where indicated.
5. Dermal tests in controversial cases.
6. Efficient treatment of the bowel to get rid of possible chronic intestinal intoxication.
7. In acute cases, the exhibition of pituitrine, adrenaline etc., etc.
8. Nasal treatment where required.
9. X-ray treatment.
10. Exercise and suitable diet.

I have a patient who can obtain relief from his asthma for long periods at a time. Whenever he feels the asthma returning, he takes to the hills, living on a low diet, sleeping under canvas, and exercising with a minimum of clothing; really leading the"primitive life". After a month or two of this, he will remain absolutely clear for a year or more.

A point of great importance is I think, to warn the patient to look out for the heavy, drowsy day. This is the time when the colloid protoplasm is getting its first shock. The moment for prompt action has arrived, and the exhibition of mercury and

salines, along with starvation and exercise will often abort an attack.

Thus the struggle to keep the protoplasm pure, may not after all be such a hopeless one; living within the limit of metabolic income, may avert the insolvency of allergy.

Hurst, however, was about right when he said, that the best way to prevent asthma was not to have it.

Bibliography.

1. Freeman. Lancet, July 31st 1920. p. 229.
2. Blackley. Experim. Researches in Asthma (1873)
3. Krogh. The Anatomy & Physiology of Capillaries 1929.
4. Adam. Asthma. p. 22.
5. Brodie and Dixon. Naus. Path. Soc. London 1903.
6. Adam. B.M.A. Annual Meeting 1929. Practitioner No. 733. 1929. p. 64.
7. Francis. The Practitioner. No. 733. 1929. p. 18.
8. Hurst. The Practitioner. No. 733. 1929. p. 4.
9. Adam. Asthma 1926. p. 4. Practitioner. No. 733. 1929. p. 62.
10. Clinical Med. Chicago 1924-25.
11. Van Leeuven. The Practitioner. No. 733. p. 27.
12. Willcox. The Practitioner. No. 733. p. 13.
13. Coke. Asthma 1923. p. 40.
14. Hartridge. Essentials of Physiology. 1912. p. 386.
15. Hansen. The Practitioner. No. 733. p. 54.
16. Dale. B.M.J. Li. p. 959.
17. Adam. Asthma. 1926. p. 4.

18. Van Leeuven. The Practitioner. No. 733.

19. Dale. B.M.J. 1923. i. pp. 959 - 1006.

20. Adam. B.M.A. Annual Meeting. 1929.

21. Krogh. The Anatomy & Physiology of the Capill. 1929. p. 220.

22. Adam. Asthma. p. 32. 1926.

23. McDonagh. The Practitioner. 733. p. 89.

24. McDonagh. " " " " "

25. Adam. B.M.A. Annual Meeting. 1929.

26. Hurst. The Practitioner. No. 733. 1929.

27. Van Leeuven. Allergic diseases also, Practitioner, No. 733.

28. Adam. Asthma. 1926. p. 79.

29. Scott. B.M.J. 1929. p. 9

30. Agar. Communication by Asthma Research Council 1929.

31. Francis. The Practitioner. No. 733. p. 68.

32. Grant. " " " " " "

33. Francis. The Practitioner. Vol. cxxiii. p. 272.

34. Hurst. The Practitioner. 733. p. 52.

.....oOo.....

A P P E N D I X.

Records of Individual Cases.

For my convenience I subdivide my cases into two groups:-

(1) Type showing marked degree of dryness of the skin.

(2) Type showing normal skin development.

One of course, notes many cases which conform to neither of these types, but which fill the intervening space between the two extremes in type.

(1) This class of case, where there is marked involvement of the skin, manifested by marked dryness and scaliness, always suggests to me that the internal secretions are to a large extent involved, probably defective secretion of the ovaries or testes, being most marked. Careful study of these patients over long periods, and confidential conversations with them on sex matters, has helped to strengthen this opinion. It is very difficult to solicit accurate or honest information from patients on certain points, which they consider, and which of course are strictly private; but I have fortunately had certain cases, where the patients, recognising that one is trying to

appreciate their "sexual feelings", was doing so, not for mere curiosity, but with desire to help them; and these cases have as I have stated, made me form the opinion, that whether primarily or otherwise there is involvement of the internal secretions.

In females this point is patent, as defective ovarian secretions produces external signs, such as defective development of the breasts, and possibly menstrual disturbances.

In the male, however, beyond a degree of asthenia and possibly "mental irritability", no definite signs may be apparent, and one must of necessity be influenced only by the history, and a very confidential history at that.

I will now give a few cases illustrative of this group.

(a) Mrs. Laurie. Aet 30 years, married. This woman was a very extreme case, and I spent many hours of the day and night in conversation with her, trying to hit upon any little point which might help me to appreciate her condition better, and perverted sexual

feelings were apparent. Intercourse was not "pleasurable" to her, and seldom desired, but she was very jealous of her husband (entirely without reason) and very exacting, almost tyrannical with him - the slightest little inattention on his part, was sufficient to induce in her an asthmatic spasm.

She had no family, had had no abortions etc., and did not desire any family - she certainly had none of the "mother-instinct". Her menstrual history was not helpful. The menstruation was scanty, and painful, but regular, and there were no signs of any gross lesions in pelvis.

Asthma developed after an attack of influenza, following long period of over-strain, while she was engaged on munition work, i.e., at time of observation it was of 5 years duration.

The skin was dry and scaly, and there was a marked amount of "powdering" of the skin.

The voice was deep and husky in tone, with frequent attacks of aphonia.

Patient had had attacks of eczema in early life.

The breasts were very small and under-developed - quite rudimentary.

Patient was markedly "neurotic", and very easily upset or offended - markedly hypersensitive, and introspective to a degree.

She seemed always happiest when she had an audience to listen to a recital of all her troubles and narrow escapes from death.

A profound asthenia was a marked feature of this case - most marked during a spasm. Loss of appetite, both during and before an attack was also a feature.

There was a definite "aura", which took the form of irritability and headache, and during a spasm twitching of face and arms, and rolling of the eyeballs was apparent. This almost resembled a true epileptiform seizure.

The only occasions on which she was free from spasms for any period, was twice when I had her removed to hospital for about 6 weeks each time.

During these two periods, she was entirely free, but on each occasion violent spasms developed immed-

iately on her return to her home surroundings.

On the few odd occasions on which she went on holiday with her own folks, the spasms were as frequent as ever.

Hereditary.

Patient's mother had suffered from slight asthma about menopause, but the family history was impossible to obtain with any degree of certainty.

Contributary factors.

Excitement, or more commonly, annoyance of any kind, was the most frequent cause.

Attacks practically constant at period.

Flowers, cosmetics etc., had no effect on patient at all, as large vases of grasses in bedroom did not induce spasm.

Patient was much attached to a dog, but after the dog was removed from the house, there was no change in her condition.

At different times I tried change of sleeping apartment, also bed and bedding, with no signs of benefit. Change of district of residence, also pro-

duced no beneficial results.

The few occasions on which patient went to an entertainment, seemed to help her by cheering her up a little.

Food.

Patient persistently kept herself on too low a diet - having been warned that diet was the cause of her asthma. I could never find any article of diet which predisposed to an attack, and when she could be persuaded to go on a fuller, mixed diet, she was if anything improved. Anorexia was, as I have mentioned a feature of this case. The bowels were always kept well regulated by patient.

Climate

Unless for the fact that the dull wet weather depressed her more than usual, I never noted any difference in her condition due to weather changes. The summer seemed to be her best time.

Periodicity.

When all her relatives, and more particularly when her husband, was at home attending her, was her

worst time - i.e., about 7 - 10 p.m.

Home Surroundings.

Her house was on a hill and always well ventilated.

The windows were kept open as much as possible- furniture was reduced to a minimum, especially in bed-room, and in fact her surroundings were little likely to predispose to allergy.

Occupation.

A little housework when able, but not often fit on account of the asthma and general weakness.

General Examination.

Height 5 ft. 3 inches. Weight 6 st. 2 lbs. Skin, dry and scaly; voice, deep and husky; breasts, small and rudimentary. There was a degree of pigmentation of the skin present.

There was a fairly persistent pharyngitis with frequent attacks of laryngitis, resulting in aphonia.

Sneezing was frequent.

Lungs. A moderate, but not marked degree of chronic bronchitis and emphysema was present, and

during the spasms the usual signs. The spasms were very severe and prolonged often lasting for 5 or 6 days, only relieved by morphia for a time, but the attack being about as bad as ever when the effect of the morphia wore off.

Patient during these attacks often appeared semi-comatose, and twitching of ~~arms~~ arms, face and rolling of eyeballs was a prominent feature. The prostration was very severe, and the pulse rate much accelerated (about 130 - 150 p.m.) Blood-pressure was often as low as 85 mm. (systolic) during spasms.

The heart sounds were pure, but of poor quality.

B.P. Systolic about 106 mm.

Diastolic about 75 mm.

Blood. Signs of secondary anaemia.

Haemoglobin 65%

Eosinophilia 3%

Wassermann reaction. negative.

Urine. Polyuria, but no evidence of sugar or albumen. S.G. 1010.

Sputum. Scanty and muco-purulent. Micrococcus catarrhalis; B. Septus, pneumococci and strep-

tococci usually present. There was no evidence of T.B. on any occasion on which sputum was tested.

Dermal Tests.

Patient gave positive reactions to a great variety of proteins, but I found no help from any dermal tests as regards treatment. She was, for instance, markedly positive to haddock and lamb - two articles of diet which she could be induced to take without bad effects as abstinence from these foods produced no results whatever. I also tried the effects of cutting off many articles which had given positive reactions, but with negative results.

X-Ray examination of chest and abdomen showed no positive findings. The sinuses were also clear.

Treatment.

Four years previous to my seeing patient, tonsillectomy was performed.

The adenoids were also removed at the same operation. Two years later the mid-turbinates were removed, and on her again consulting a specialist on my advice, submucus resection of the nasal septum was

tried. Neither of these operations, I am sorry to say, had any beneficial effects, unless the fact that she was a "nose-breather" can be credited to one of them.

Like all asthmatics, patient had tried all sorts of patent "cures" - inhalations, mixtures for coughs etc., etc.

Tucker's inhaler, with its spray of cocaine and atropine was her constant companion, and it certainly did give her temporary relief at times, although during her spasm it had not the least effect.

Strict dietary, and regulation of the bowels was always practised by patient. For the relief of spasms, pituitrine and adrenaline were helpful, although morphia had always to be given also, sometimes 3 - 4 injections.

I tried this patient on injections of peptones, prepared from the proteins to which she showed positive reaction, but I noted no results whatever. I then gave her a course of standardised mixed peptones, but the results were also negligable. Autogenous vaccines

even given over long periods, I did not find helped to any appreciable extent, nor did mixed stock vaccines (P.D.& Co,) although I did think that the latter helped the bronchitis a little.

Change of air and environment had no lasting beneficial results, nor had any drug tried, and I tried all the usual remedies, e.g., Mg.Ki, iodine, arsenic preparations used in syphilis etc. I even went the length of having this patient seen by a psychologist of repute, but beyond the fact that he agreed, that the mental condition was somewhat similar to that sometimes noted in cases of menopausal mental disturbances, we had no satisfaction.

Large doses of ovarian substance given by the mouth, gave I think the best results, but very large and continuous doses, were not easily tolerated by the stomach. The administration of mixed gland preparations did not appear to help much. An attack of broncho-pneumonia following an attack of asthma and bronchitis, unfortunately carried this patient off.

The main outstanding features of this case, were

the absence of any results from treatment - the extremely intractable nature of the condition, and the definite "mental disturbance" present.

Before the development of the asthma, the patient evidently was a bright, healthy subject.

Dr. A.F.Hurst's definition of asthma, "that asthma is due to an over-excitable broncho-motor portion of the vagus nucleus, due to blood borne irritants, or to peripheral or psychical stimulants"; i.e., due to some disturbance of the central nervous system, seems attractive after cases like the above.

I have noted a good many other cases, not quite so marked as the above quoted certainly, which force one to the same conclusion. I have seen cases, where the asthma only developed about the menopause, or at the corresponding "climax" in male cases, where the marked "mental disturbance" was very evident.

These cases I have found answer excellently to injections of ovarian or testicular extracts respectively. Some of them in fact respond remarkably quickly. The above facts, force one to consider the

endocrine glands as a possible cause - some imbalance, such as that which occurs at the menopause, with the resultant mental disturbances. Or it may be as Dr. A.F.Hurst would suggest, that the lesion of the central nervous system is primary, and the endocrine disturbance the exciting cause.

Of course, in a condition with such an enormous number of symptoms as "allergy", one cannot come to conclusions readily, but I think it is reasonable to suppose, that at least in some cases the "protein-poison" affects the endocrine glands, and the resultant imbalance produced in the glands, would cause the nervous symptoms etc., and produce cases like the one quoted.

The following case is somewhat similar to the last case, but it has been chosen as it shows the same features, but not in such an extreme form. It suggests the same cause or causes, but the lesser degree of sexual underdevelopment and mental disturbance present, illustrates the gradual transition from the extreme type, to the types where no symptoms may

suggest the endocrine glands as a possible cause.

(b) Mrs Titman. Aet. 32 years. Married.

Asthma developed about puberty, following influenza. Patient was introspective and neurotic, and subject to fits of crying and depression.

Menstruation was irregular, patient sometimes missing one or two periods, but there was no evidence of any lesion of uterus or adnexa.

Sexual intercourse was not much desired, and always followed by breathlessness, increased depression, and tendency to spasm. Patient had no family, and was not interested in children. She had never been pregnant.

The skin was dry and scaly, and the voice deep and husky. The breasts were small and underdeveloped. A degree of pharyngitis was present, and attacks of laryngitis were frequent. She was much troubled with "common colds".

Generally patient was languid, but during and after spasms, asthenic was very marked. Patient's general outlook was much better than that of the pre-

vious case.

The "aura" took the form of marked asthenia with headache.

Rolling of eyeballs, asthenia, and tachycardia were present during spasms, and during the most severe spasms, patient was prostrated and semi-comatose.

Hereditary.

Maternal uncle had asthma, and her mother suffered from recurrent attacks of eczema.

Contributary factors.

Patient considered chills to be the cause of her attacks. Attacks were frequent about menstrual periods, and after sexual intercourse.

Worry also played a part, because if patient did not receive her usual letters from Australia, where her relatives resided, she was very likely to have a bad turn.

Pollens, cosmetics etc., did not, as far as we could ascertain, do her any harm, nor did theatres etc.

There were no animals in the home.

Food.

Patient carefully regulated her diet and bowels. Potatoes alone seemed to affect her, by increasing the wheeziness.

Climate

Patient was born in Australia, and remained there until she was 25 years of age. The asthma began there, and although on medical advice she tried many parts of Australia, she did not find relief. She also was advised to go to sea with her father, who was a ship's captain, and she did this for twelve months. The asthma was not appreciably relieved at sea.

South Africa was next tried, and she remained there for about 4 years, but with no benefit to her asthma.

Her husband obtained a position in Scotland, and the asthma still continued unabated, so it was manifest that climate had no effect on her condition. On each occasion she changed her country of residence, there was a few months of temporary improvement; but

as soon as she became acclimatised to the country, the attacks became as frequent as ever.

I tried the effect of having her residing in a high part of the country, where the air was excellent, and then having her residence changed to a low-lying part, below the level of the Clyde, but really did not notice any appreciable difference in her condition.

Periodicity.

I could not really say that I could name any definite time, perhaps because the spasms were always preceded by bronchitis.

Home Surroundings.

Were always good. Plenty of fresh air, with a minimum of furniture etc.

Occupation.

Patient took a fair amount of walking exercise, and did some housework.

General examination.

Height, 5ft 3inches. Weight 10st. 5lbs. Patient was well-formed, except for the lack of development of breasts. Skin dry and scaly. Voice deep and

husky. Pigmentation present, but not marked. A chronic pharyngitis was present.

Lungs.

There was evidence of fairly marked chronic bronchitis and emphysema, and during spasms the usual asthmatic signs were present. The spasms were severe after lasting 2 - 3 days. There was marked prostration and tachycardia during attacks.

The B.P. fell to about the region of 90 m.m. during spasms, and the pulse rate was about 110 - 130 p.m.

B.P. Systolic 110 m.m.

Diastolic 85 m.m.

Blood. Signs of secondary anaemia

Haemoglobin 75%

Eosinophilia 3.2%

Wassermann reaction negative.

Sputum. Tenacious, muco-purulent and scanty.

No evidence of T.B. Micrococcus Catarrhalis, B. septus and streptococci (haemol) found.

Urine. Increased frequency, but no evidence of abnormal constituents.

Dermal Tests. Positive to potatoes, and sole, but at times the scarifying alone gave positive reaction, so that the tests were not of value.

X-rays. Examination of chest by X-rays showed no positive findings. Frontal sinus and antrum were clear.

Treatment. The nasal mucous membrane had been twice cauterised in Australia.

On my advice a specialist was consulted and tonsillectomy and removal of turbinates was advised, and duly carried out. There were no good results from these measures apparent.

The usual long list of remedies for asthma had been gone through - inhalations, dietary treatment etc., but the spasms were not alleviated.

I had patient in hospital, where dermal tests were carried through, and the appropriate peptones prepared and injected, but no lasting benefit was obtained. I tried mixed peptone injections with the same results.

Autogenous vaccine was given over long periods, and on not noting improvement, I gave her a mixed stock Bronchitis vaccine (P.D.& Co.), and this seemed to improve the bronchitis, and therefore help a little.

During the spasms one had to fall back on morphia, with adrenaline ~~with~~ and pituitrine. Mercury, the iodides etc., etc. were exhibited without avail, and latterly I commenced giving daily injections of adrenaline and ovarian substance, also mixed gland (female) tablets orally. I continued this treatment for about three months.

The general condition certainly improved considerably, also the skin, while the spasms were certainly not so severe, and I think considerably less frequent. After the 3 months, I discontinued the injections, but kept up the oral treatment. The diet was carefully watched, also the bowels. Unfortunately patient had to return to Australia, so that I have been unable to ascertain if the improvement was maintained, but during the time she remained in Scotland, which was for about 6 months after the injections

were stopped, patient seemed to be improved. I advised her to continue oral medicine indefinitely.

I have seen and noted a good number of cases of this type, all more or less similar to the two given.

There was of course, a variable degree of sexual underdevelopment and nervousness present, but stated generally, the main features of this type of case are:-

1. Dry-scaly skin.
2. Deep toned, husky voice.
3. The underdeveloped breasts.
4. The absence of pregnancy and the perverted sexual feelings.
5. The marked asthenia associated with the spasms.
6. The nervous, introspective disposition.
7. The intractable nature of the asthma, and the absence of benefit from nasal operations.

The above case would seem to bear out the facts noted in Case 1.

The question is, whether the "Allergic Inheritance" is an imbalance between the endocrine glands, or is the disturbance of the endocrine glands the result

of the "protein poison".

I will now refer to two female juvenile cases of the dry-skinned type.

One cannot, of course, see the same evidences of gland defect in children, as is natural from the undeveloped condition of a child's body, but certain features of these cases, make it convenient to place them in this group.

c. Betty Hill. Aet 5 years.

Child developed asthma when about one year old. The asthma seemed to be the outcome of bronchitis.

When two weeks old the child developed bad infantile eczema, extending over both arms and head. The skin was very dry and scaly. Child was from birth extremely irritable and difficult to feed. She was "snuffly", and always seemed to have catarrh in head.

Her weight was a little below normal, but not very much.

Vomiting her feeds was common.

Hereditary.

Child's father was an asthmatic of the dry-skinned type.

Her paternal great-grandfather was also an asthmatic.

It is of interest to note here, that I saw the child's father, who as I have mentioned was an asthmatic of the dry-skinned type, when he was 16 years of age. He had suffered from asthma for 2 years at that time.

Long continued (3 months) injections of pituitrin and adrenalin, along with the oral administration of testicular extract and mixed gland tablets, caused his spasms to gradually cease, and they so far have not recurred. The only occasions on which he feels a little wheezy, is following sexual intercourse.

Contributary factors.

Asthmatic spasms always seemed to follow some obscure chill, and were always accompanied by bronchitis.

Child was easily upset by any little disorder

of stomach or bowel.

Climate.

Asthmatic spasms were worse in cold, wet weather, probably because the bronchitis was worse at those times.

Periodicity.

No special time noted.

Home surroundings.

Good - plenty of fresh air and attention to diet and bowels.

General examination.

Well formed child, but skin dry and scaly, with frequent recurrences of the eczema.

The voice was particularly low toned and husky.

Child was a little prematurely old looking.

Chest. A fairly marked degree of chronic bronchitis and emphysema present.

The usual rhonchi etc., noted during an attack, which was always accompanied by bronchitis. Child was much prostrated during attacks and pulse rate much accelerated. The heart sounds were pure.

Blood. Haemoglobin 70% Wasserman reaction was negative.

Eosinophilia 2.5%

Sputum. The sputum was scanty, muco-purulent and tenacious. There was no evidence of T.B. Pneumococci, and staphylococcus albus were found.

Urine. No abnormality noted.

Treatment. There was no evidence of any abnormality requiring treatment in throat or nose (specialist's report).

I at first tried the usual expectorant mixtures, but they were of no avail. An autogenous vaccine did not seem to help much.

I then tried bi-weekly injections of pituitrine and adrenaline for 3 months, along with small doses of ovarian, thyroid and pituitary extracts by the mouth. The oral treatment was persisted in for about 12 months, and weekly injections given for 3 months longer.

The general condition of the child quickly began to improve, also the skin, and although for a time the spasms continued, they were less severe. By the end

of about 4 months the skin condition was about normal, and the spasms had practically ceased. The child has remained free, in spite of having had broncho-pneumonia.

d. Miss. McWhirter. Aet. 7 years.

Child developed first signs of asthma when about 3 years of age.

The asthma seemed to be the outcome of bronchitis. Child was very subject to colds in head.

She was a little underweight, and very nervous and had an anxious, wistful expression, not at all childlike. Skin was dry, but not scaly. Voice deep toned and husky and attacks of laryngitis were frequent.

Subject to periodic attacks of conjunctivitis.

Heredity.

Paternal grandfather had asthma. Child's mother has progressive muscular atrophy.

Contributary factors.

Attacks usually associated with chills, but indiscretions in feeding predisposed to attacks,

especially sweets and potatoes.

Uninfluenced by pollens, etc., cat which was kept was expelled, but no difference was noted.

Changes of sleeping apartment, bed etc., did not produce any change in condition.

Food.

Sweets and potatoes, i.e., an excess of carbohydrates in diet predisposed to attacks.

Climate.

Change of air and variations in weather did not as far as I could see, make much difference.

Periodicity.

Spasms usually during the night.

Home surroundings.

Were of the best. Plenty of fresh air, good food and warm clothing.

Occupation.

Child was at school, and able to attend fairly regularly. I also tried as much as possible to have the child out and playing with other children at games etc.

General examination.

Child was a little underweight. Skin - dry. Voice deep and husky.

Chest. A fair degree of bronchitis and emphysema present. During the spasms, which were always accompanied by bronchitis, the usual dyspnoea etc., was apparent.

Asthenia was marked during apasms and tachycardia was prominent.

The heart sounds were pure.

Blood. Secondary anaemia present.

Haemoglobin 75%

Eosinophila 3%

Wassermann reaction negative.

Sputum. Scanty and muco-purulent. No evidence of T.B., only a few streptococci found.

Urine. No albumen or sugar. Urea diminished during spasm.

Dermal Tests. Positive to potatoes, and other foods rich in carbohydrates.

Treatment. Tonsils and adenoids removed when child was 5 years. There was no evidence of

amelioration of symptoms as result of operation.

Parents had tried all the usual patent remedies, and many orthodox ones besides.

Diet and bowels were regulated, and parents warned against allowing excess of carbohydrate foods.

Peptone injections did not show any good results, nor did an autogenous vaccine. A course of mixed bronchial-asthma vaccine (P.D. & Co) seemed to relieve the bronchitis a little.

I then tried my usual treatment with children, i.e., bi-weekly injections of pituitrine and adrenalin for 3 months, and weekly injections for an additional 3 months or so. Along with this, I give orally, ovarian (or testicular) thyroid and pituitary extracts for long continued periods.

In the present case, the attacks gradually lessened in severity, later in frequency, and after about 6 months, disappeared, and have not shown any signs of recurring.

Before claiming credit for the treatment, it is only fair to give full consideration to the possible

effect of the regulation of diet and bowels, which I always point out the importance of, to the parents.

I also advise parents to allow the children out with the other children to play etc., and to help them to lead as normal an existence as possible, as the effect of being as it were, "kept in cotton wool" in my opinion has a very bad effect on the child's nervous system, and tends to make one introspective etc.

The following two cases are examples of the dry-skinned type in males.

(e) Master Anderson. Aet 14 years.

Child developed asthma at the age of 10 years. A thin, dry-skinned, prematurely old looking child.

The voice was low-toned and harsh, or rather croaky. There was marked powdering of the skin.

Child was nervous and morose. Before attacks there was the "aura", consisting of vomiting and headache. To sum it up the child was like, and behaved like a nice, old man.

Hereditary.

Mother was an asthmatic of the dry-skinned type. Maternal grandmother has bronchitis and marked rheumatoid arthritis.

Contributary factors.

Chills induced bronchitis, which in turn led on to asthma.

Excitement of school such as a scolding from teacher always led to an attack.

Flowers, grasses, cats etc., did not appear to affect child.

Change of air, bedroom etc., also appeared to have no lasting good effects.

Food.

Mother had previously been carefully and efficiently instructed about dietary and bowel regulation, which advice she followed closely, being a sufferer herself. The child, however, as children will, would frequently eat too many sweets and on these occasions a spasm was always in the offing.

Climate.

Patient was worse during the winter, as his bronchitis was more frequent and severe then.

Periodicity.

The early morning, about 2 - 4 a.m. was the commonest time of his spasms.

Home surroundings.

Were healthy. Air clean and fresh, with absence in the home of excess of furniture.

Occupation.

School-boy; but unfortunately patient was often absent, as he was so hypersensitive to discipline etc., and so often unable to attend owing to his bronchitis.

General examination.

Small, wizened, prematurely old-looking child. Dry, scaly skin and deep croaky voice. A degree of pigmentation noted. Sneezing was frequent.

Chest. A fairly marked degree of chronic bronchitis and emphysema present, both between and during acute attacks of asthma.

Spasms were severe, and they were accompanied by

marked degree of prostration.

Tachycardia was a feature and there was profuse perspiration during spasms. The B.P. was always also low.

Blood. Haemoglobin 70% Wassermann reaction negative.
Eosinophilia 4%

Sputum. Tenacious, muco-purulent and scanty. No evidence of T.B., and only the usual catarrhal organisms found.

Urine. Increased frequency - child had always to rise once or twice during night. Urea decreased during attacks. No other evidence of disease of kidney or bladder.

Dermal Tests. Marked multiple positivity - showing such a variety of reactions, that tests seemed to me to be of no value.

Treatment. According to specialist, no active treatment for throat and nose was indicated. Patient's mother being an asthmatic, she was well versed in the various 'cures', and the poor child was for ever being made swallow medicine, or inhale medicated vapours. etc.

I tried mixed peptones, but with no benefit.

An autogenous vaccine certainly helped the bronchitis, and the general condition of the patient also benefited.

The course of treatment which I have already stated, I give as routine to children, answered extremely well in this case. The skin and general condition of the patient improved, as did the bronchitis and the asthma, and except for an occasional slight bronchitis, the child has remained clear.

The next case to which I will refer, is an adult male. He, I think falls under the above category.

I have sandwiched the juvenile cases in between the adult cases, for the sake of the contrast in regard to the results of treatment; my opinion being, that if the defect can be artificially remedied for a time in the child, whose endocrine glands etc., are impressionable, and in a state of active growth, the wonderful power and adaptibility of nature, which is always striving to keep all the various organs in a

ADDENDA .

It may be , that the improvement in some cases following the regular administration of pituitrine and adrenaline , ~~and~~ is due to the fact that these glands are made to grow, by a process of excitation.

The greater success of this treatment in children being due to the fact that the undeveloped glands of children are naturally more easily influenced.

Dr. G. W. Crile of Cleveland Clinical Foundation, Cleveland Ohio. U. S. A. by his work on hypothyroidism, has demonstrated that by feeding thyroid extract, the sluggish inactive thyroid can be made to grow. This is probably also the case with other Endocrine Glands.

Great care has to be taken and careful watch kept on the metabolism. I have only once , however, seen any untoward result where the pituitrine and adrenaline was administered with caution, and that was the developement of exophthaline goitre in a man after prolonged treatment.

state of perfect balance and harmony, will be stimulated to restore the balance of the endocrine glands, or whatever organ, secretion etc., is at fault. (See addn'l).

(f) Mr Goodwin. Married. Aet. 50 years.

Developed asthma after pneumonia, when 40 years of age.

This was an extremely severe case, and patient was quite unfit for work of any kind owing to the frequency of the attacks, and the profound degree of asthenic which followed. Patient was very nervous, introspective and irritable.

Patient looked much older than his years. All sexual desire was gone.

The skin was dry and scaly, and the voice deep in tone and husky.

Profuse perspiration was common, accompanied by attacks of tachycardia.

Any little annoyance predisposed to spasm.

The "aura" took the form of headache and profound asthenia.

Patient had, he thought, had eczema in childhood.

Heredity.

Maternal uncle had asthma. Patient's family all appeared to be healthy.

Contributary factors.

Annoyance of any kind certainly predisposed to attacks of asthma. Colds, which increased his bronchitis also predisposed.

On the odd occasions on which patient had intercourse, a spasm was almost certain to follow the next day.

Pollens, cosmetics etc., did not as far as I could see affect him, nor did public meetings etc., as long as he was not irritated. Patient kept two cats, which I had removed, after much heated argument, but their removal did not help. At different times I tried change of house, of bedroom, bed, mattress etc., but could not really say I noticed any difference.

Food.

Patient kept himself on a very strict dietary, and paid great attention to regulation of bowels etc. In fact he was far too interested in his general

anatomy and his complaint, to be healthy.

Excess of carbohydrates in dietary certainly made him "wheezy". Meat he would not touch, as he stated that he had bad effects from eating it.

No other articles of diet seemed to affect him adversely.

Climate.

This patient is rather interesting as regards climatic influence.

He resided in various parts of Scotland and England, but unless for the fact that with every change he made, he had a period of temporary improvement, no benefit was obtained.

Foolishly perhaps, but because while in South Africa I had seen one or two asthmatics who had improved with residence there, I advised him, as he had relatives in Durban to try the change. All during the voyage he was very bad indeed, and also when he arrived there - so bad in fact, that in about six months he returned to Scotland.

Home surroundings.

Were very healthy, and not likely to predispose

to allergy.

Occupation.

For the last few years he was unfit for work of any kind. Previous to that he had been a master-joiner.

General Examination.

Height 5ft 8 ins. Weight 8st.10 lbs. Patient was prematurely old looking, and had extremely anxious expression. Skin dry and scaly; voice deep and husky. There was a pharyngitis present, sneezing was frequent, and attacks of aphonia common.

Pigmentation was fairly marked.

Chest. Marked degree of chronic bronchitis and emphysema present. During the spasms, which were always accompanied by an acute exacerbation of his bronchitis, tachycardia was marked.

There was a V.S. mitral murmur present, and the heart sounds were of poor quality.

The spasms were very severe and prolonged, and patient was much prostrated.

The systolic B.P. was often as low as 85 m.m.

B.P. Systolic 97 m.m.

Diastolic 80 m.m.

Blood. Fairly severe secondary anaemia.

Haemoglobin 60% Wasermann reaction negative.

Eosinophilia 5%

Urine. Urates decreased during spasms.

S.G. 1013.

No albumen - no sugar.

Sputum. Muco-purulent, scanty, during spasms, but fairly profuse at other times.

Micrococcus Catarrhalis, B. Septus, and streptococci found. No evidence of T.B. at any time.

Dermal Tests. Extensive dermal tests done in hospital, where I may mention patient did have spasms.

The appropriate peptones were tried, but had no beneficial effect.

X-Ray. No evidence of disease noted except a degree of fibrosis of lungs.

Treatment.

Tonsillectomy had been performed when disease

was of one year's duration,but had produced no beneficial results. The following year the nasal mucous membrane was cauterised.

Patient had tried all the usual medicines, inhalations etc., etc. but with no beneficial effects. The absence of benefit from change of climate I have already mentioned.

Peptones, vaccines etc., I tried,but with no good results. Testicular extract and other extracts of endocrine glands were exhibited without any apparent benefit. Pituitrine, adrenaline and morphia relieved the spasms, but I may say that all the treatment I gave did not do any more than give him temporary relief.

Patient died of capillary bronchitis and bronchopneumonia, following a very severe bout of asthma.

I have given fairly severe cases of the dry-skinned type only, but have noted various modified degrees of this type.

Adult cases of this type I have found most intractable, while the juvenile cases I have seen, have

answered most satisfactorily to treatment.

Of course, conclusions cannot be come to as result of the very limited number of cases one can meet with in private practice.

(2) Type showing normal skin development.

It may seem that I am, by this subdivision of my cases, trying to make out two distinct types of asthma, but such is not my idea.

The majority of cases are mixtures of these types, showing no definite signs of sexual underdevelopment etc.

Each individual case must differ, as each individual has colloids peculiar to himself - the individuality being in the colloids.

(a) Mrs Govan. Aet 42 years. Married.

Asthma developed at the age of 32 years, following "feverish attack", following abortion.

Patient was a normally healthy minded woman, who had 6 children. She was very interested in her family and her home. Sexual desire was present, but

always tended to maker her "wheezy".

Menstrual history was uneventful, and there was no evidence of any gross lesion of uterus, etc.

Patient was stout and puffy, with a very fine healthy skin. The voice was deep and croaky.

The breasts were well-developed. The "aura" took the form of general malaise, with increased breathlessness.

Patient was in hospital for 2 months having dermal tests etc., done, and during her residence there, had 3 severe attacks of asthma.

Heredity

Father had asthma. Patient's second son developed asthma of the dry-skinned type at age of 14 years. He died at age of 24 years of acute pulmonary tuberculosis. The remainder of her family are healthy, except her eldest daughter who is subject to rheumatism.

Contributary factors.

"Chills" which increased her bronchitis, seemed to predispose most to attacks. Patient states that

early in her illness she had hay-fever, but this had now passed off, and patient was not affected by pollens etc., as she was really better in summer, as her bronchitis was improved then.

Patient had an intolerance to aspirin. Domestic animals of which she was very fond were removed, but no benefit was noted. Meetings, etc., did not adversely affect her.

Food.

Carbohydrates in excess in diet certainly predisposed to spasm, but no other articles of diet seemed to produce bad effects.

Climate.

Patient had relatives in the South of England, and stated that she was always much better while residing there, probably because the more kindly climate helped her bronchitis. She was, as I have stated, better during the summer weather.

Periodicity.

Spasms usually occurred during the night.

Home surroundings.

Very healthy, and hygienic.

Occupation.

Patient did most of her own housework, and on my advice had walk of a few miles daily.

General Examination.

Height 5 ft. 6 ins. Weight 13st. 5lbs. Skin healthy; voice deep, and breasts well developed. No pigmentation.

Attacks of aphonia common, as also was sneezing. Chest. Marked signs of chronic bronchitis and emphysema, and spasms always accompanied by an acute exacerbation of the bronchitis. The spasms often lasted for several days.

Patient had complete anorexia during spasms, and there was a fairly marked degree of prostration present. Tachycardia (130 - 150 p.m.) was also a feature.

The B.P. during spasms was in the region of 95 m.m. The heart sounds were pure.

B.P. Systolic 120 m.m.

Diastolic 85 m.m.

Blood. Haemoglobin 75% Wassermann reaction negative.
Eosinophilia 4%

Urine. Increased frequency of micturition, but no evidence of disease of kidneys in bladder.

Sputum. Scanty and muco-purulent. No evidence of T.B., streptococci, B. septus and staphylococcus albus found.

Dermal Tests.

Markedly positive to potatoes, cod fish, sole, tomatoes, but the exhibition of the particular peptones did not benefit, although I thought that the injection of mixed peptones helped.

X-ray. Examination revealed no signs of disease.

Treatment. Tonsillectomy had been performed, but no benefit felt. She was a mouth breather.

She had as usual tried all the usual remedies, and Tucker's inhaler was her constant ally, and did give her temporary relief, unless during the severe attacks when recourse to pituitrine and adrenaline was necessary. Morphia had very bad effect on her.

A long course of an autogenous vaccine helped

the bronchitis a little.

A course of injections of ovarian extract, and mixed gland tablets orally, seemed also to give a degree of relief.

The general health was certainly improved. By the regular use of mercurials and salines, and strict regulation of diet, and a moderate amount of exercise this patient could keep fairly comfortable.

(b) Mrs White. Aet 35 years. Married.

Asthma developed when patient was 20 years of age. She states that an attack of pneumonia was succeeded by a bronchitis, which in turn developed into asthma. Patient "highly-strung", but anxious to work and not be an invalid. Outlook on life healthy.

At times patient states she has peculiar abhorrence of sexual intercourse, and she always feels the worse of any connection, which increases her breathlessness, and tends to induce spasms.

She has one child, a boy of 14 who has unfortunately inherited her asthma. He has normally healthy skin, and his asthma is associated with bronchitis.

Patient is well-formed; skin clear and healthy, breasts well developed; voice of deep tone. Patient is subject to violent fits of temper. In fact the "aura" takes the form of headache with extreme irritability.

Subject to head-colds and sneezing.

This patient's mentality is much above the normal, and she is most anxious to do her work, and sometimes carries on when very breathless and ill.

A marked degree of asthenia associated with the spasms.

Heredity.

No definite history could be obtained. Patient's child aged 14 years has asthma of the healthy-skinned type.

Contributary factors.

Attacks always associated with acute bronchitis, which follows colds. Patient was usually most liable to attacks at period. Attacks most frequent in the summer, when vegetation was at its height.

Patient extremely fond of cats, but the removal

of these pets did not benefit her condition. They are now re-instated in favour.

Food.

Excess of carbohydrates in diet tended to make patient more wheezy, but no other articles of diet seemed to produce bad effects.

Climate.

Patient had resided for two years in Germany. She had also resided in various districts of Scotland, and also in the south of England, but unless for the fact that she was always temporarily benefited by the change, no permanent good resulted.

She was under treatment for 6 months, at Davos in Switzerland, but derived no permanent benefit.

On other occasions she was in nursing homes under specialist treatment, with rigid dietary etc., but on her resuming her normal life the condition returned as of old.

Periodicity.

Attacks were always associated with bronchitis, and were certainly usually most aggravated during the

night.

Home surroundings.

Patient had undergone so much expert treatment, as regards diet, hygiene etc., that she conducted her home almost along hospital lines.

There was a minimum of furniture etc., and open air was the order of the day.

Occupation.

Housework and walking. Patient when fit, also interested herself in outside social affairs.

General examination.

Height 5ft. 7ins. Weight 12st. 3lbs. Well formed breasts, healthy skin and deep voice.

Patient was subject to recurrent attacks of laryngitis. There was a chronic granular-pharyngitis present.

Chest. There were marked signs of chronic bronchitis and emphysema, and the spasms which sometimes lasted for 2 - 3 days were always associated with bronchitis. Patient was markedly prostrated during spasms, and anorexia and very dirty tongue were features.

The B.P. was low during attacks, about 95 m.m. and a degree of tachycardia was also present. The heart sounds were pure and of fair quality.

B.P. Systolic 115 m.m.

Diastolic 90 m.m.

Blood Signs of moderate degree of secondary anaemia. Haemoglobin 75% Wassermann reaction. Eosinophilia 2% negative.

Urine. Polyuria. S.G. 1012. Decreased urea during spasms. No albumen - no sugar.

Sputum. Scanty and tenacious at all times. Pneumococci, streptococci haemol; found. No evidence of T.B.

Dermal Tests. Patient had been a patient in a London nursing home, where much experiment had been carried out on her with skin tests.

She had also had series of peptone injections there, and as she did not feel any benefit, she was unwilling to undergo further dermal tests.

X-ray examination of chest, abdomen, and face, revealed no evidence of disease.

Treatment.

Patient who was in good circumstances had undergone much treatment.

Changes of climate to Davos etc., course of starvation ~~and~~ or at least strict dietary in homes, vaccines, peptones etc., etc.

Her tonsils had been removed, nose cauterised on two occasions, but without any appreciable benefit resulting. She had undergone treatment with massage, and "the waters" at various spas, and had had various pollen vaccines tried.

Tucker's inhaler was used daily, and patient had an hypodermic syringe with which she gave herself injections of pituitrine and adrenaline when required, but morphia had always to be exhibited during spasms.

Strict regulation of diet, with injections of ovarian extract and mixed gland extracts orally over long period (4 months) certainly improved her general condition, and the spasms were not so frequent.

It is interesting to note that on three separate occasions, I tried this patient on small doses of

Luminol, and each occasion the result was violent and prolonged spasms.

I will now quote two juvenile cases. Children of this group I have usually found to be fat, chubby, "lymphatic" looking subjects, and a strong contrast to the prematurely old looking children of Group 1.

(c) Miss Stewart. Aet 6 years. Developed asthma at age of 4 years. Patient had had recurrent attacks of bronchitis for a year or two previous.

Child was fat and flabby, just like an advertisement for a patent food.

Very subject to colds in head and sneezing, and to fits of crying - that inconsolable type of crying, probably really hysteria in the very young.

The voice was deep, and the skin clear and healthy.

A "crying fit" seemed to serve as an aura. Stomach was easily upset, and child required a great deal of attention.

Heredity.

No definite history of allergic manifestation

obtainable. Father had chronic bronchitis while Mother was extremely nervous, and subject to attacks of paroxysmal tachycardia.

Contributary factors.

Colds and dietary indiscretions the most frequent cause of the spasms, especially sweets. The usual intolerance to carbohydrates so often noted.

Flowers etc., did not affect the child. There were no domestic animals.

Food.

As stated carbohydrate excess predisposed to spasms. Diet and bowels had always to be closely watched, as any indiscretion was inclined to induce spasms.

Climate.

Child worse during winter as bronchitis was worse then.

Periodicity.

Always between 2 - 4 a.m. and accompanied by hysterical crying.

Home surroundings were very good. Plenty of fresh

air etc.

General Examination.

Child fat, flabby and really over healthy looking. The type of child one would have qualms about administering $CHCl_3$ to, suggestive of "status lymphaticus".

Skin in very healthy condition, and voice distinctly deep in tone.

Child of nervous, irritable disposition. Heart of good tone and sounds pure.

Chest. Chest barrel shaped, and signs of bronchitis and emphysema present. During the spasms child very jumpy and nervous.

Blood Haemoglobin 90% Wassermann reaction negative.
Eosinophilia 3%

Urine. No evidence of any disease of kidneys or bladder. S. G. 1013.

Sputum. Very scanty and tenacious. No evidence of T.B., only a few pneumococci found.

Dermal Tests. Positive reaction to potatoes and oranges only, but results really not satisfactory. An attempt to desensitive child to those articles of diet was not successful.

Treatment.

Tonsils were enlarged, but parents would not permit of any interference. Bronchitis had been treated by the usual poultices, expectorant mixtures etc., and it was only when the spasms began to keep the parents up all night, that they would consent to vaccines, adrenaline etc., being injected. A mixed vaccine helped the bronchitis a little, but peptones had no effect.

Bi-weekly injections of pituitrine and adrenaline for three months, along with ovarian extract orally was next tried. Strict attention to bowels and diet was also advised. Very soon the spasms became less frequent and less severe, and after about 3 months, entirely disappeared.

There are occasionally slight recurrences of the bronchitis but not of the asthma.

This patient is now 14 years of age, and is a healthy normal child, well fitted to take her place in life.

(b) Master Christie. Aet. 6 years.

Developed asthma at the age of 3 years. Child

nervous,and of a distinctly "lymphatic" type.

Skin clear and healthy,but child too fat and flabby. No evidence of any "aura", but as an attack of bronchitis always preceded the spasm it is difficult to say.

Heredity.

Father had chronic bronchitis and mild asthma. Elder brother had had infantile eczema, but no further history could be obtained.

Contributary factors.

Mainly due to colds,as attacks were always preceded by bronchitis.

Excess of carbohydrates in diet was certainly a predisposing cause. Child was very sensitive,and parents though that excitement tended to induce spasms.

Food.

Child passionately fond of sweets, and all sugary food, but as stated,excess of carbohydrate diet very quickly caused the stomach to be upset,and at these times a spasm was always imminent.

Climate.

Worse during cold wet weather, when of course the bronchitis was at its worst. Had not the chance of seeing the effect of a warm sunny climate as parents could not afford it.

Periodicty.

Attacks much more frequent during the night.

Home surroundings.

Healthy with plenty of fresh air etc.

General Examination.

A real "picture of health" looking child; fat, fair and flabby;-wheezing on the least exertion. Voice inclined to be husky and low pitched. Skin of very fine texture and colour.

Chest. Well marked emphysema, and signs of chronic bronchitis present.

Usual physical signs during the spasms, with marked degree of irritability and nervousness. The heart sounds were pure but soft. Child always passed urine involuntarily during spasms . Mouth breathing was the rule.

Blood. Haemoglobin 80% Wassermann reaction was negative.
Eosinophilia 3.5%

Sputum. Scanty. No evidence of T.B. Pneumococci, Pneumobacilli, and micrococcus catarrhalis found.

Urine. Apparently normal, but urea diminished during spasms. Earlier in life bed-wetting had been very persistent.

Dermal Tests. I am afraid that either owing to peculiarity in the subject, or to defective technique, the results were of no value. Plain cold water even gave a positive reaction, and practically every protein tried did likewise.

Treatment. Specialist did not consider that any active treatment of throat or nose was advisable or necessary.

Parents had tried many remedies; inhalations etc., etc. but without alleviating the condition in any way. An autogenous vaccine along with the usual exhibition of pituitrine and adrenaline, with testicular substance was tried, and this along with regula-

tion of bowel and diet, caused a cessation of spasms in about four months.

I have been in touch with this case for many years, and there has been no recurrence.

It will be seen that both types of child cases although so markedly different in physical features, both reacted to the same treatment.

In my opinion both types force one to consider the endocrine glands as the possible cause.

(e) Mr McCartney. Aet 36 years. Married.

Patient states that he developed asthma after a severe attack of bronchitis when he was 16 years of age. This patient was a very deep thinking and intelligent man, and very willing to give one every help he could, in appreciating his case and his feelings. He had one child, and was keenly interested in his work and home.

Sexual intercourse was enjoyed, but he always was wheezy for a day or two following.

He was morbidly interested in medical affairs, and well versed in psychological literature etc.

Patient was an enthusiast in all things he set his hand to. Public speaking was one of his chief joys, and he became so very excited over his speech, and the preparations for it, that he either developed an attack of asthma and could not attend the function, or had to be bolstered up with large doses of bromides to check his excitement a little. On these occasions, when he really reached the meeting, in the words of my district, "he spoke like an apostle".

The skin was healthy, and the voice distinctly husky.

The "aura" was very indefinite; he just had feeling of impending disaster, and he was markedly prostrated during spasms. Involuntary emission of semen frequent.

Heredity.

No satisfactory history obtainable. Child had T.B. cervical glands.

Contributary factors.

Patient was very fond of motor cycling, as he considered that it gave the maximum of fresh air. He

was probably right, but in addition it gave him acute attacks of bronchitis, which in turn produced asthma.

Excitement, sexual or otherwise was a strong predisposing cause.

As far as we could ascertain, flowers, cosmetics etc., had no bad effects, nor had attendance at meetings, theatres, etc., as long as he was not taking any active part.

Food.

An overloaded stomach was a distinct predisposing cause, and any excess of carbohydrate diet specially so.

Climate.

Worse in dull, wintry weather. On two occasions, when patient had an extended holiday in south of England he stated that he was considerably better.

Periodicity.

Attacks most frequent in the early hours of the morning.

Home surroundings. Healthy and hygienic.

Occupation. Patient was a house factor, but had

plenty of exercise. He was a very energetic man.

General examination.

Height 5ft 11ins. Weight 12st. A well built, well coloured, healthy looking man.

Chest. Marked signs of chronic bronchitis and emphysema, which bronchitis was always acute during spasms.

The spasms were very severe and often lasted 2 - 3 days. Before and after spasms, tongue was dirty and anorexia marked.

B.P. during attacks was low, 90 - 100. The heart sounds were pure and of good quality.

B.P. Systolic 130 m.m.

Diastolic 95 m.m.

Blood. Haemoglobin 85% Wassermann reaction negative.

Eosinophilia 4%

Urine. Polyuria before and after attacks with decrease of urea during attacks. Faint trace of albumen usually present, but no sugar or other abnormal constituents.

Sputum. Fairly profuse and muco-purulent. Streptococci, B. septus, staphylococcus albus found. No

evidence of T.B.

Dermal Tests. Patient had exhaustive dermal tests done in hospital, and the appropriate peptones injected, but without any apparent benefit.

X-rays. There was no evidence of disease, except a few scattered patches of fibrosis in lungs.

Treatment. Earlier in the course of the disease tonsillectomy had been performed, also cauterisation of nasal septum, but the results had been negligable.

Nasal surgeon did not consider any further treatment advisable.

This patient was a perfect "walking encyclopoedia" on all matters pertaining to asthma and its treatment.

One could not mention any thing, that he was not familiar with, from the benefits of high altitudes, to protein desensitisation and psychological treatment. He really only tolerated my advice and treatment, when he was too prostrated to treat himself.

During spasms the usual remedies gave relief. Peptones were of no avail. An autogenous vaccine did help his bronchitis, and I thought that a course of

injections of testicular extract also helped. The general condition most certainly was benefited.

However, psychology appealed most to him, and he, with my permission, placed himself in the hands of a doctor in London who, at that time, was being much "boomed" by the newspapers, so much so that the unfortunate practitioner's name was later removed from the register.

The main item of treatment seemed to be the training of the patient to practise "self-control", and according to my patient, it was most efficiently and impressively taught. My patient came back to the home town ready to proclaim his marvellous cure from the housetops, so that every sufferer could be marvellously delivered as he had been from their "form of insanity". In truth, I must own that he most certainly was improved. When he had an attack after that, he would not even own up that it was a recurrence, and would go to sleep with his morphia, praising his marvellous deliverance. Of course, one could easily see the benefit of the "self-control" practice in a neurotic subject.

.....oOo.....

The following table is an attempt to summarise briefly the cases given.

Type (1) Adult.	Type (2) Adult.
1. Dry scaly skin.	Healthy, normal skin.
2. Deep-husky voice.	Deep - husky voice.
3. Sexual underdevelopment.	Normal sex development.
4. Sexual desire not strong or absent.	Sexual desire not so markedly affected.
5. Sexual excitement predisposing to spasms.	Same.
6. Marked asthenia.	Asthenia not so marked.
7. Intractable to treatment.	Not so intractable.
Type (1) Juvenile.	**Type(11) Juvenile.**
1. Dry scaly-skin.	Healthy skin.
2. Deep voice.	Deep voice.
3. Thin, anxious, prematurely old looking child.	Fat, chubby, healthy looking child.
4. Amenable to treatment.	Same.