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ASTHMA AND ALLIED
CONDITIONS.

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So much has been written about asthma and its ætiology has been looked at from so many viewpoints, all of which, I suspect, reveal portions of the whole truth, that it is necessary to give some sort of confession of faith before making observations which must be regarded as one's own. All that I say will not be accepted by all present, but I have the consolation of knowing that you are all fully qualified to hold your own opinions and to denounce mine.

Derivation.—Greek ἀσθμα, gasping, panting, applied by Hippocrates to the ailment we know as asthma¹.

¹ C. H. Armbruster, scholar and philologist, has given me the following note: The word ἀσθμα, panting, used by Æschylus and Plato, then applied by Hippocrates to this ailment. *Hipp. Aph.* 1248, *et al.*

Clinical Definition.—We associate the term asthma with paroxysms of embarrassed respiration followed by longer or shorter periods of complete calm, and with recurrences at more or less frequent intervals.

This definition would correspond to many cases of asthma but not to all. It would apply to what was termed true or spasmodic asthma, but the other form, chronic bronchitis or bronchial catarrh, with exacerbations of asthma, so-called bronchial asthma would not be included.

Modification of Definition Needed.—The clinical description needs modification to include the cases where the dyspnœa is continuous and paroxysms of increased dyspnœa are brought on by slight exertion, and to include the many cases where there are no paroxysms at all.

For reasons which I will state later, I hold that the terms “chronic bronchitis” and “bronchial catarrh,” as we use them, should not be used at all when speaking about asthma, they are misleading.

The dyspnœa of asthma is both inspiratory and expiratory, more especially the latter, the expiratory phase of respiration being

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incomplete and prolonged; the chest is distended and over-distended and the diaphragm immobile; in a severe attack the patient appears to breathe entirely by the accessory muscles of respiration in order to increase the capacity of the chest in his effort to obtain interchange between stagnating alveolar air and the atmosphere.

Now there are many steps between a little early morning wheeziness, which none the less is asthma, and the following distressing clinical picture which describes a severe spasmodic paroxysm:—

The pale, anxious, perspiring face, the livid countenance, the prominent forehead veins, the bulging eyes, the head fixed in position, and the powerful back muscles dense and contracted, in order to aid in the respiratory effort. This is a well known condition. The patient sits with arms fixed to his chair to bring into play the extraordinary expiratory muscles. His breath whistling and wheezing, he utters his words with difficulty. The thorax almost motionless, the respirations may become extraordinarily slowed. Inspiration is difficult because the chest is over-distended already, expiration is more difficult on account of the obstruction in the bronchioles.

An attack may last for an hour or for days. In the interval between the attacks the patient may be quite at ease.

It used to be said that, notwithstanding the distressing character of the attacks, asthma is not one of the diseases which shorten life.

So far as it goes this clinical description is correct, but it is only one part of the whole picture, and I think the less important, and the less serious.

In the child asthma is usually periodic in its recurrence, but as he grows older the ailment tends to become more erratic in its manifestations and in its times of appearance. Though at first it may be strictly spasmodic, later it is attended by what is known as "chronic bronchitis."

But let me at once state that the syndrome

we call asthma has two parts, the spasmodic action of the muscular constricting fibres of the bronchioles and the turgescence or vaso-secretory swelling of the mucous membrane of the bronchi in varying proportions. Sometimes the spasm, sometimes the turgescence predominates, almost, perhaps, to the exclusion of the other, but sometimes both are equally balanced.

Asthma was described in 1923 by an authority as "a volume full of unsolved problems" (Coke).

Another authority in 1930 wrote "The problems of asthma are most baffling, recent work has cleared the ground and defined the issues" (Langdon Brown).

A. F. Hurst, at the 1929 Manchester Meeting of the British Medical Association, commenting on the fact that it was the sixth occasion on which asthma had come up for discussion at an Annual Meeting, doubted whether any real advance had been made, but he believed that the disease was better understood than heretofore. And the writer of a special article in the *British Medical Journal*, April 27, 1929, stated that, "in spite of the great activity displayed in this country, in America, and on the Continent, there were as many uncured asthmatics and as many so-called cures, and this in spite of—I think he wrote, *owing to*—the fact that more has been written on asthma than on any other ailment.

Well, that is the state of affairs to-day. All we can say is that the disease is better understood than heretofore.

The eminent Guy's Hospital physician, Goodhart, in his article on Asthma ("A System of Medicine," Clifford Allbutt, 1898, vol. v), describes it as a clinical entity of unknown cause, with two separate manifestations, the idiopathic dry, spasmodic asthma, and the secondary form which originated in chronic bronchitis; and he mentions three theories concerning its morbid anatomy.

Theory 1.—The theory most generally held thirty years ago was that the paroxysm was

caused by the muscular constriction of small bronchioles.

Theory 2.—In order to accord with the physical signs and symptoms, Sir Andrew Clark, Blackley and others held that a rapid swelling of the bronchial mucous membrane of a non-inflammatory nature took place during an attack—a swelling, they said, analogous to urticaria, and similar to that which takes place in the nasal mucous membrane in a cold or in hay fever.

There was a third theory more difficult to maintain—it has gone to the wall now, but it had its supporters thirty years ago—that the paroxysm was due to sudden collapse or atelectasis pulmonum through plugging of bronchi with mucus.

The stethoscope, the action of drugs and the discovery of muscular fibres in the bronchi by Reisseisen, confirmed by the experimental work of Brodie and Dixon in 1921, established the muscular constriction theory, together with the close association between the mucous membrane of the nose and the bronchial muscular fibres; and the investigations of Huber and Koessler¹ in 1922 on the morbid anatomy of six asthmatics, who died in a paroxysm, or from some other cause, who found definite hypertrophy of the muscular coat of the bronchi and bronchioles together with hypertrophied mucous glands and hyperæmia of the mucous membranes, support the second theory.

Both the theories of thirty years ago regarding the morbid anatomy of asthma, have been shown by dissection to be correct—both, I repeat, together form the morbid anatomy of asthma.

Next a discovery was made, or published, in 1910, which advanced knowledge regarding the cause of the morbid anatomy of asthma. Dr. Bryan Melland² found that adrenalin injected subcutaneously relieved

the paroxysms of asthma. The action of adrenalin on any part is the same as stimulation of the sympathetic fibres to that part (Langley), constricting the involuntary fibres, and as the action of the sympathetic fibres is antagonistic to the vagus (parasympathetic), the theory that asthma was due to overaction of the vagus nerve appeared to be established, in fact the ailment asthma was a *vagotonia*.

How do we stand to-day?

We know the morbid anatomy of asthma—constriction of the lesser bronchi and bronchioles, together with a vaso- and secretory-motor turgescence of the mucous membrane of the bronchi and bronchioles, in varying proportions, and that this is brought about by the action of the vagal nucleus.

Our present knowledge of asthma is well expressed in a formula by Langdon Brown,¹ improved, as he states, by A. L. Hurst:—

“Asthma is due to an unstable or irritable condition of the bronchomotor portion of the vagus nucleus which causes it to react unduly to psychical and peripheral stimuli or to foreign proteins in the circulating blood,” and he includes the obvious vasomotor turgescence which accompanies the vasomotor spasm, as this is always present and is sometimes the most striking feature of an attack, just as it is in the closely allied condition of hay fever.”

Langdon Brown's Diagram.—By the following diagram Langdon Brown illustrates the above formula:—

¹ W. Langdon Brown and R. Hilton, “Physiological Principles in Treatment.” Sixth Edition. 1930.

¹ H. L. Huber and K. K. Koessler, *Arch. Int. Med.*, xxx, pp. 689, 1922.

² B. Melland, *Lancet*, 1910, i, 1407.

Having stated these facts we have gone as far as we are able to go without entering the region of theory and speculation. But why, we may ask, is the vagus centre unduly irritable? Why should sights, frights, disappointments, odours, thoughts, precipitate paroxysms of asthma?

Why do peripheral stimuli such as digestive disturbances, uterine disorders, morbid conditions of the nasal cavity and sinuses, enlarged hilum glands, bring on an attack? Digestive disturbances may of course sometimes be due to a vagotonia of the gastric mucous membrane.

What is the explanation of the fact that certain drugs such as aspirin and ipecacuanha, pyramidon, will determine an attack? Contrarywise, aspirin sometimes cuts short an attack.

Why do "foreign proteins"¹ circulating in the blood bring about an attack? Why should loss of balance as between the endocrine secretions appear to favour an attack?

The fact is, we know many causes which excite a paroxysm of asthma, but the fundamental and basic cause remains obscured.

I believe that the most important fact we know about asthma is that it is an *hereditary* ailment. Asthma appears to spring from an hereditary flaw and an hereditary cause must be metabolic. We can imagine that the cells of the vagal nucleus were hereditarily functionally weak, but we may with equal logic picture the vagal centre cells irritable because they were not supplied with an appropriate pabulum, or supplied with a toxin owing to the failure of metabolism elsewhere.

Whatever reply is given to the question, what is the fundamental cause, it should include and embrace all the controversial views; we must seek a solution in complex

biochemical processes not completely understood.

Many an interesting problem is connected with asthma. It is a disorder of civilization; uncivilized races and wild animals are not asthmatic. Man and some domesticated animals, pig, dog, parrot, are subject to it. Man differs in habits from animals who do not get asthma in the preparation of his food. This suggests, it has been suggested, that the cooking of food by civilized nations plays a part.

An interesting fact about asthma is that frequently it occurs for the first time suddenly late in life. A clergyman who had spent many years in Tropical Africa got his first attack of asthma suddenly (July, 1928) whilst on furlough, when he was 64—on the Euston platform on arrival from Liverpool one night at 10 p.m. He was carrying a suitcase, which he had to put down. He has had asthma now (November, 1930) almost continuously for over two years—nothing so far relieves him excepting adrenalin and rest in bed. No locality or climate has had any good effect.

In his case, so far we have failed to discover that any relative or forebear of his suffered from asthma.

This would appear to be a notable exception to the hereditary factor in asthma.

Asthma is periodic, especially at the beginning. For years it comes at a particular season. Fortnightly attacks are common, and also week-end; a paroxysm may come on every evening after going to bed—1 or 2 o'clock in the early morning is a usual time, wheezing in the early morning on rising is a common manifestation.

Women frequently have severe paroxysms at the monthly period. In fact, asthma is periodic or rhythmic.

Rhythm.—Shipley says ("Life," p. 5), "Living matter is rhythmic," and he devotes a whole chapter (XII) to "Rhythm in Cells, Tissue Organs, Organisms and Communities."

Asthma is rhythmic, it is concerned with

¹ Certain foreign substances in the air, grass pollen, dust of ipecacuanha, sandal-wood, rose-wood, face powder (orris root), moulds (*Aspergillus fumigatus*), may bring on a paroxysm; animal emanations, cats, dogs, horses, feathers, another exciting cause.

the biochemical processes of certain tissues; these processes are determined by heredity or by the pabulum they derive through the circulation. The various organs and tissues of the body are so co-ordinated and inter-dependent that it is not possible to say which organ or tissue is primarily to blame in asthma.

CAUSES OF ASTHMA.

With regard to the fundamental and basic cause of asthma, we are completely in the dark.

No one theory satisfactorily accounts for all the facts — we look to biochemistry for the key to the solution, though so far biochemistry has not been able to solve the problem.

In the meantime a fault in the metabolic processes of the organism appears to be the nearest accurate explanation, an explanation which falls in with the anatomical picture—the spasm of the bronchioles, the swelling of the bronchial mucous membrane due to the increased irritability of the vagal nucleus and nerve, irritable because they are starving, they are not supplied with a “food” they require, or they are intoxicated by a food they cannot use for their metabolism.¹

If we consider that the vagal nucleus is defective by inheritance we may approximate the truth, but we should not leave out of account the question whether the vagal centre irritability may not be brought about also by the incapacity of other tissues and organs hereditarily at fault. The metabolism of the liver may be at fault, producing toxic proteins; the metabolism of the alimentary-canal may be at fault, producing toxic bodies instead of tissue foods; the meta-

bolism of certain endocrine glands may be hereditarily at fault. In this sense the endocrine glands have been suspected to be the cause (thyroid, parathyroid, suprarenal glands) by hypo- or hyper-activity, but there is nothing conclusively to incriminate the ductless glands.

The vagal nucleus may be hypersensitive in one case of asthma from one cause, in another case from another cause. The same cause may not be acting in every case.

In the meanwhile until biochemistry offers a more detailed explanation we must be satisfied with this broad *metabolic* view, for it includes all of the well-known theories and is antagonistic to none. It accounts for certain proteins inducing an attack, the anaphylactic or allergic view.

It appears to account for certain localities being free from asthma, for the psychological causes of an attack, why climate is a predominating factor, why foods, chemical stimuli, drugs induce a paroxysm.

We must take a comprehensive view, general enough to include all the recognized theories, each of which appears to account for a group of cases, but not all cases; the basic cause to be convincing must hold good for every case.

HEREDITY.

One of the most important facts of asthma is this hereditary predisposition.

Hyde Salter in 1868 made out a *clear hereditary history* in 39 per cent. of 217 cases.

Dr. James Adams found 25 per cent. of his 153 cases gave a history of inheriting the predisposition.

Other observers have found a higher percentage:—

The Edinburgh Committee (*Lancet*, 1929, vol. i, p. 517), found that 38·7 per cent. were hereditary.

Coke, 46 per cent. of 550 cases.

Adkinson (“Genetics,” July 5, 1920, quoted in Norris and Landis’ “Diseases of the Chest”) gives 48 per cent. in a series of cases numbering 400.

¹ “Applied Biochemistry,” Withrow Morse (W. B. Saunders and Co.), 1925, p. 369. The introduction of quamin into the blood-stream experimentally causes spasm of the bronchioles (asthma). Following parathyroidectomy guanidin and methyl guanidin occur in the urine. Are we therefore right in assuming that asthma is due to parathyroid deficiency? Is asthma due to hypo- and hyperactivity of an endocrine gland?

Hurst notes that this frequency of hereditary history is too great to be accidental, and asks, "What is it that is inherited?" And he answers "Sometimes it is the irritable bronchial centre, sometimes toxic idiopathy, sometimes both."

I do not think this reply by itself is sufficiently inclusive. But there is no doubt that the fundamental cause of asthma is inherited.

If cases of "Chronic Bronchitis" under the heading "Bronchial Asthma" were included, as I think they should be, I maintain that many cases now labelled "Chronic Bronchitis" are asthma manifesting the second part of the asthma syndrome—turgescence of the bronchial mucous membrane; the percentage of inheritance would be vastly higher and the inherited factor in asthma would be still more obvious if more people knew their family medical history.

A case I saw recently in Out-patients'—a girl, aged 25—had her first paroxysm at the age of 19, after an attack of influenza. Neither father nor mother nor any of their own family, excepting the patient, had asthma or bronchitis, but the mother had a mental breakdown. The father's mother died of bronchitis and the mother's father had bronchitis, and the mother's grandfather died of asthma. This is one of many examples which bring out the relationship between asthma and chronic bronchitis. But why is the fact of heredity in asthma important?

(1) An inherited disposition is due to a

Dr. Morris H. Kelm in the *Archives of Internal Medicine*, May, 1927, published by the American Medical Association, Chicago, reviews the present conceptions with regard to the status of curability of bronchial asthma.

Prof. Karl Hausen (*Proc. Roy. Soc. Med.*, April, 1929) suggests another possibility, interesting but vague, and visionary as it appears to me—psycho-analytical—the *hereditary* deficiency in an act. I will leave this argument to psychologists. It is interesting but it includes only a few cases.

flaw in the metabolic activity of a tissue or organ. It explains:—

(2) Why the only hope of a definite cure for asthma (I do not mean temporary relief) lies in ability to remedy the metabolic disability, which must naturally be a long process. We must not expect to discover a sensational (in the sense of speedy) cure for asthma.

SODIUM IODIDE AS A REMEDY IN ASTHMA.

When speaking of a remedy for asthma, one must clearly have in mind the two separate states: a patient in the acute paroxysm and the same patient in his ordinary everyday state between the paroxysms, perhaps breathing quite normally, but not cured of his asthma.

It cannot be said that a patient is cured until taking his chances as an ordinary individual his asthma does not recur.

The paroxysms of asthma may be dealt with effectively in two ways: by relieving them with adrenalin when they occur, or by ascertaining the exciting cause and eliminating it; for example, avoiding an article of food which induces an attack, by seeking a place of residence (Switzerland) where the exciting cause is not present. Neither of these methods deals with the fundamental or basic situation. Sodium and potassium iodide have little effect on the paroxysm of asthma, but they deal, I think, with the basic cause.

The basic cause of asthma is an hereditary flaw in the metabolism of a tissue, organ or group of cells.

Can we do anything to deal with an hereditary flaw in metabolism? It is not an easy question to answer; we do not know in the case of asthma whether the defect is in the vagus nucleus itself or in a tissue or organ on which the vagus nucleus relies. The blood feeding the vagal nucleus obtains its stock of nourishment, which it distributes, from various sources: a contribution from the endocrine glands, another from organs such as the liver, from the

intestine, and from elsewhere. The sources are many and varied, and failure from one or other of those sources might explain the irritability of the vagal centre—the argument is speculative, and I will not pursue it. One of the remedies recently advocated in the treatment of asthma, and used with success, especially for children, is *glucose*, and the subject of asthma has lately been approached with ingenuity and success in children at Great Ormond Street, from the point of view of the HCl content of the gastric contents. These facts suggest a fault in the metabolism of an organ.

Broadly speaking, food consists of the following chemical compounds: protein, fat, carbohydrates, water, certain bodies we call vitamins, *inorganic salts*. It is a striking fact that all of these receive a great deal of attention from our profession, except *salts*; yet it is known that the simple inorganic salt, readily broken up into its elemental units, has its uses in the building up of living tissues, although it may not actually be found in the final composition of protoplasm. Shipley wrote: "Salts come within the compass of one definition of food: whatever sustains and supports growth."¹

Now, potassium iodide usually forms one item of the prescriptions for asthma in most hospital pharmacopœias. Osler looked on pot. iodide as specific for asthma ("Practice of Medicine").

These facts, and certain biological facts relating to iodine, which there is no time to mention to-day, led me in 1921 to try in the Out-patient Department whether pot. iod. used in larger quantities than the usual might not prove successful in treating asthma. I tried it intravenously, but pot. iod.² gives pain when intravenously injected, so I substituted sod. iodide.

Intravenous injection of sod. iod. was advocated in America for the treatment of asthma in 1921 (B. R. Loewy, *Amer. Journ. Clin. Med.*). Now the B.P. dose of sod. iod. is 5 to 20 gr. Its toxicity is low; it is diuretic and expectorant; very soluble, 2 gr. dissolve in 1 min. water, therefore 60 gr. are well dissolved in 1 drm. of water. Although the B.P. dose is 5 to 20 gr., by commencing with small doses we have the authority of Howard, writing in the *Amer. Journ. of Syphilis*, 1918, that as much as 1 dr. four times daily may be given by the mouth over a considerable period, and according to American literature (Howard, *Amer. Journ. of Syphilis*, 1918), it is stated that "much larger doses can be tolerated intravenously than orally." Further, intravenous injections of sod. iod. are stated to be more lasting than oral administration.

Sod. iod. by the mouth appears in the urine in 10 to 25 minutes, and is present in the urine for two to seven days. Accepting Sollman's figures ("A Manual of Pharmacology," 2nd edition, p. 820), 0.8 grm. per kilo is the lethal experimental dose for sod. iodide. Therefore 1 drm. of sod. iod., which is the maximum dose I give for intravenous injection in cases of asthma, is well within the experimental lethal dose.

Sod. iod. has been used for syphilis, goitre, tuberculous ulcers and for *asthma*.

In asthma one must be circumspect when speaking about a cure—remedy is a better word to use. There is no doubt that some

cannot be used intravenously proves a difference. They have not the same solubility. Sod. iodide contains more iodine than pot. iodide. See D. Lueen and A. K. Konwiser, "Intravenous Therapy," January, 1926, p. 7. No doubt the iodine of pot. iod. and sod. iod. is the principal constituent. Iodine stimulates metabolism generally, apart from the fact that it appears as a constituent of the *thyroid* where it occurs in small quantities. Small quantities are sufficient for the metabolism of the thyroid gland. In large doses, 3 or 4 drm. daily, pot. iod. is specific for actinomycosis. Iodine appears necessary for animal metabolism.

¹ "Life," Shipley, 2nd edition, p. 58.

² Sod. iod. is not often used nowadays, it is considered to be inert; its uses are said to be similar to pot. iod. and its action the same, but neither of these statements is true. The fact that pot. iod.

cases of asthma do extremely well on sod. iod., and some severe cases have in my experience apparently been cured after a prolonged course. Perhaps you will say *post hoc ergo propter hoc*.

Boch (*Colorado Medicine*, September, 1926) cites his own case and the cases of ten patients where the treatment was successful, but the details he gives are meagre. The method I favour in the adult is a bi-weekly intravenous injection of 30 to 40 gr. NaI in 20 c.c. of water. The treatment to have permanent effect should be continued over a long period, perhaps months, but in the meantime the paroxysms are controlled.

Sod. iod. may also advantageously be given by the mouth, 30 gr. at 6 p.m. and at bed-time is useful and efficacious in asthma; 20 gr. in water may be given three times daily; 20 gr. at 6 p.m. and at bed-time, or 20 gr. three times daily is not too much for children of, say, 5 or 7 years old.

To some the taste of sod. iod. is unpleasant and metallic. Occasionally one comes across a person unable to take it, even in small doses, producing as it does sometimes headaches, nasal catarrh, pustular rash. But only occasionally a patient shows, after large doses over a long period, what may be termed mild toxic effects.

Loss of voice, attacks of coryza, lachrymation, salivation, headache (frontal sinus)—symptoms not in themselves serious.

In one case of mine, a boy, aged 9 (Skipp), attacks of paleness, dilated pupils, faintness, appeared to follow; they might possibly have been due to sod. iod., but when the drug was re-continued after an interval, in the same doses, no untoward symptoms appeared and the asthma improved greatly.

Amongst toxic indications not frequently met with may be mentioned (to complete the list):—

Rigor, chilliness, dryness of the throat, œdema of eyelids, papular or pustular rash, bleeding of the nose—hæmaturia.

Excepting an occasional pseudo-rigor, or complaint of chilliness, none of the above

have occurred amongst my intravenous injections—therefore I advocate intravenous injections of sod. iod.

It has been calculated that 65 per cent. of the dose of sod. iodide is excreted by the kidneys in twenty-four hours, the remainder in two to seven days.

How does sod. iodide act?

Neither the sodium nor the iodine appears to remain within the body.

The sodium is probably a convenient mate for the iodine, which appears to be necessary for normal metabolism. The thyroid is the only tissue in the body having an appreciable amount of iodine in its composition, but it is unlikely that asthma is to be explained as thyroid derangement. The thyroid is certainly enlarged in some cases of asthma, but not in many, and symptoms of hyper- or hypo-thyroidism are not common.

Thyroid extract neither cures nor aggravates asthma.

Inorganic salts are necessary to metabolism, their rôle is often overlooked. This may be the answer to the question, How does NaI act in asthma? If it is true that sod. iodide acts beneficially, then broadly speaking one may look on sod. iod. as a food substitute for a starving vagus centre, or for a group of cells not functioning normally elsewhere; and acting on this theory, I have given, and give now in certain cases, sodium iodide and glucose at the same time.

ASTHMA AND CHRONIC BRONCHITIS.

The study of contemporary writings of medical men in the professional journals for the last few years reveals no advance in the knowledge and treatment of the disease known as "chronic bronchitis." Is it because there is nothing new to write about? Is the medical profession confronted with a hopeless condition, or are we, unconsciously, gradually arriving at the conclusion already held by certain American writers, that the

state which is called "chronic bronchitis" is not a disease *sui generis*?

The existence of a certain morbid state characterized by epithelial changes, sero-cellular exudation, emphysema of the lung, changes in the bony thorax, and, finally, cardiac changes, is not open to question; but are we right in using the word "bronchitis" as a cause of the changes?¹ Is what we term "chronic bronchitis" fundamentally a bronchitis or indeed an independent disease?

The older textbooks classify bronchitis as acute and chronic—and name subdivisions according to the character of the sputum. But apart from these there was and is described a disease, "chronic bronchitis." It is given a class to itself and, with its sequelæ, it takes a high place amongst serious diseases. A visit to the Poor Law Hospitals reveals that many of the old men and women there are suffering from it in varying degrees of severity, and in time most of these old men and women will, directly or indirectly, die from it.

In the out-patient rooms of the chest hospitals there is no disease more frequently met with, and none whose outlook is more hopeless. But in order to be in a position to deal successfully with a disease, it is necessary to know its primary cause and to tackle it in its early stages.

There is considerable uncertainty with regard to the fundamental and basic causes of the group of chest disorders, asthma, bronchitis and asthma, bronchial catarrh, chronic bronchitis, and bronchial asthma. The frequency with which they are associated itself suggests that their association together may not be fortuitous, that under

several names we have, perhaps, various manifestations of one underlying disease.

In the asthma syndrome there is muscular constriction of the bronchioles and also vaso- and secretory motor swelling of the bronchial mucous membrane. If we concentrate on the anatomical picture, which we know to exist in asthma, we are on firm ground, and it is possible we may find answer to the question, Why does so-called chronic bronchitis so often complicate asthma? Is it the bronchitis which by sensitizing the organism to a foreign protein produces the *asthma*; that is to say, have we to deal with two separate diseases, or are we dealing with one disease which has two manifestations, a muscular and cellulo-secretory?

Those who have worked in the out-patients departments of special chest hospitals see many cases of dyspnoea with wheezing rhonchus and sibilant râles, and diagnose "chronic bronchitis." They frequently have reached a state of permanent incapacity.

Owing to greater facilities for examination provided by X-rays and electrocardiograph, more can now be done than formerly for these patients, but modern appliances have thrown light on the effects of chronic bronchitis rather than on the causes.

We can interpret the amount of fibrosis, emphysema and myocardial disease, we diagnose bronchiectasis, we associate chronic bronchitis with barrel-shaped, rigid chests, dusky complexion betokening seriously embarrassed heart and breathing, particularly expiration laboured and noisy.

But such patients are suffering from sequelæ—emphysema and possibly myocardial disease; the original ailment is overshadowed by the end-results.

Very little can be done by treatment for emphysema and consequent cardiac disease, because changes in thorax, lungs and heart are irreparable. But, after all, these are the end-results of a long-continued morbid condition.

It is safe to say that in every case there

¹ No doubt the bronchi may be invaded with the organism of inflammation. Acute bronchitis may go on to subacute and chronic bronchitis. One may have bronchopneumonia and chronic inflammatory conditions due to mechanical particles in the air (inhalation bronchitis), but these are not what is known as "chronic bronchitis."

was a time when the patient suffered only from so-called "chronic bronchitis." It is highly important to state this, because the time to treat an incurable disease like emphysema is before structural changes occur—it is the early so-called chronic bronchitis that we must treat. If this is a part of the asthma syndrome then we must concentrate on asthma to get rid of chronic bronchitis and emphysema. It is important to know whether we are dealing with two diseases or one, with asthma and bronchitis, or asthma alone.

The Name.—Certain writers refuse to recognize the existence of a primary chronic bronchitis under any circumstances ("Diseases of the Chest," Norris and Landis, B. 268). I confess to being sceptical, and I would suggest a not altogether original view, but one not generally held in England, that what we call chronic bronchitis in the beginning is not primarily an inflammatory condition at all, it is not primarily a disease of the air passages, it is the part of the asthma syndrome which is always more or less present in cases of asthma, namely the vaso-secretory swelling of the bronchial mucous membrane. I will enumerate one or two facts which appear to support this view:—

Chronic bronchitis is inherited, a disease passed on from father to son. This alone would make us suspect it was not originally an inflammation. In "chronic bronchitis" the classical signs of inflammation are themselves absent, there is no rise of temperature. Chronic bronchitis, like asthma, is periodic and fluctuating and lasts a longer period of time than inflammations do.

In many cases of chronic bronchitis the clinical picture is asthma where the bronchitic symptoms, and turgescence of the bronchial mucous membrane, overshadow the muscular spasm of the bronchi. Cases which commence as chronic bronchitis go on to typical paroxysmal attacks of asthma. The two states have many things in common. Chronic bronchitis sometimes begins in infancy, it frequently recurs year after year, it

is periodic, it is progressive, it has the complications and sequelæ of bronchial asthma, and the remedy which in my experience is often effective in asthma is often effective in chronic bronchitis, namely, sodium or potassium iodide.

The same remedy for what is really the same disease. Finally, the microscopic appearance of sections of chronic bronchitis are consistent with a non-inflammatory sero-cellular condition.

In conclusion, I am inclined to think that we overlook an important part of the asthma syndrome, namely, the vaso-secretory turgescence of the bronchial mucous membrane and submucous tissue, and that the chronic bronchitis which so often accompanies and complicates asthma is primarily not a chronic bronchitis at all, but the clinical manifestation of the second part of the syndrome (the first part being muscular constriction).

FEVER OF OBSCURE ORIGIN IN CHILDHOOD.

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WITH the gradual advance of medical knowledge and the increasing help obtainable from the laboratory, the diagnosis of obscure fever is becoming somewhat simplified. Such terms as "febricula" are no longer in use, yet it served as a useful though rather unsatisfactory name for certain of the unexplained fevers of the last century. It is true that in the Great War, when the exigencies of the moment often demanded a hasty label for a case without sufficient time for proper diagnosis, P.U.O. (pyrexia of unknown origin) was a particularly popular classification. Such a diagnosis to-day would rightly be looked