BRITISH MEDICAL JOURNAL

LONDON SATURDAY SEPTEMBER 28 1946

SOME VULGAR ERRORS IN REGARD TO GOITRE

BY

J. W. LINNELL, M.D., F.R.C.P. GEOFFREY KEYNES, M.D., F.R.C.S.

AND

J. E. PIERCY, F.R.C.S.Ed.*

During the past generation the importance of goitre as a fount of many unsuspected ills has become more and more recognized. It is but natural that new advances in any field of medicine should only gradually become known to the profession at large, and goitre is no exception to the rule. It is with the object of discussing some of the commoner fallacies concerning its dangers, diagnosis, and treatment that we who have had the opportunity of studying the condition over a long period of years venture to write this article. We would say it was the intention of the late Cecil Joll, who worked at our clinic throughout the war, to collaborate with us in its production, and that, though death prevented his doing so, he had already expressed his complete approval of the plan and the opinions embodied in it.

I. That, though goitres which are patently toxic need treatment, the great majority of the rest are harmless or practically harmless, will probably remain so, and may safely be left untreated

By a curious coincidence an article in the *Journal of the American Medical Association,* entitled "Potential Dangers of Nontoxic Goiter," by Cole, Slaughter, and Rossiter (1945), was published almost simultaneously with one written by Linnell (1945) in the *Practitioner,* entitled "The 'Harmless' Goitre," which ran on much the same lines. Both drew attention to the danger of such complications as (1) the development of thyrotoxicosis with its many and multifarious complications, (2) carcinomatous changes, and (3) pressure through increasing size. These complications are discussed in greater detail below. In the discussion which followed the reading of the American paper one speaker stressed the risk of sudden pressure by haemorrhage into the substance of the gland—a somewhat rare complication—though this point had not gone unnoticed by us.

1. *Thyrotoxicosis.*—The common belief that comparatively few goitres become toxic has no foundation in fact. The American workers we have mentioned believe that no less than 50% of all non-toxic goitres become toxic if left untreated, and add that, in view of the narrowness of gradation between non-toxic and toxic nodular goitres, this figure may well be too low. We, for our part, believe with Hertzler (1936), and many other workers in different parts of the world, that by the time early middle life is reached goitres without some evidence of associated toxicity are rare. It would seem that most medical practitioners recognize only the gross and more easily discernible symptoms and signs of thyrotoxicosis; those of less degree go unrecognized or are disregarded as being of little importance. These symptoms, it may be said, often can only be detected by careful observation, for they may amount to no more than some of the following: lassitude, minor or occasional palpitations, slight irritability or emotional instability, loss of weight, irregular sweatings or feelings of heat, a small rise of the resting or, better, sleeping pulse rate, a fine digital tremor, the suspicion of a stare due to retraction of the upper lids, and an almost imperceptible difference in the size of the palpebral fissures. The fact that there may be phases of exacerbation and intermission of the symptoms does not make their discovery easier. As to their being of little consequence, it cannot be too strongly emphasized that they are of the greatest importance. Unfortunately, it is not yet generally appreciated that next to acute rheumatism toxic goitre is the most fruitful cause of auricular fibrillation, and goitres of apparently such mild toxicity as we have described are, without any doubt whatever, often responsible for it. In this connexion it may be well to add that occasionally auricular fibrillation has been, in our experience, *apparently* the very first sign of toxic change. Other signs were no doubt there, but were so slight as to escape observation. Toxic goitre, whatever the degree of toxicity, can also cause auricular flutter, both paroxysmal and established, and auricular paroxysmal tachycardia; but these are relatively rare complications.

To exemplify the frequency of auricular fibrillation as a complication of toxic goitre Papp (1945) says that 20% of all patients with toxic goitre develop this symptom, and that, though it is exceptional under the age of 30 and uncommon between 30 and 40, it becomes increasingly frequent thereafter, so that 80% of all cases of thyrotoxicosis fibrillate after the age of 60. These figures are sufficiently arresting, and our only comment is that, as the significance of the milder degrees of thyrotoxicosis is more widely recognized, it will almost certainly be found that the total percentage of patients who develop fibrillation is considerably higher. Generally the fibrillation is at first paroxysmal and only later established—a matter, as we shall see, of considerable importance; and the fact that established auricular fibrillation is a forerunner of congestive failure must never be forgotten.

2. *Carcinomatous Change.*—American workers are evidently very much more concerned about this danger than we on this side of the Atlantic. In the article already referred to it is stated that no less than 7.2% of 523 non-toxic goitres of all kinds operated on were found to be carcinomatous, and that among single non-toxic nodules as many as 24% were so affected. Lahey, the chief of the famous clinic of that name, in the discussion which followed the reading of the article, insisted that neither the size of the goitre nor the age of the patient mattered; that he had known a boy of 9 die of carcinoma of the thyroid, and that he had had several patients with the same condition at 12, 13, and 14 years of age. This would fit in with the belief held by many that most carcinomas of the thyroid derive from foetal adenomas: a belief, however, that is incapable of proof, as by the time mid-life is reached the tumour has, as a rule, suffered so much change through growth and haemorrhages into its substance that it is impossible to be sure as to its original structure.

We must confess that we have so far seen no carcinomas in children, though several have occurred in quite young people. The majority have been in patients of middle life or later. Still, there are a disconcerting number of patients in this country whose goitres are allowed to become patently carcinomatous before they are deemed to be proper subjects for surgery; and we would insist that by the time the

* Members of the L.C.C. Thyroid Clinic.

textbook picture of carcinoma of the thyroid is present the growth has penetrated the capsule and invaded the surrounding tissues, so that as a rule the hope of a surgical cure is past, even if by surgery and deep *x*-ray therapy life can often be prolonged for many years. It is lamentable to see, as we have seen, patients with widespread secondaries who have, over a long period of years, been urged not to worry about their goitres, and have continued to receive this advice even though they were steadily increasing in size and fixity and sometimes causing a sense of pressure or even pain. We would stress that tenderness on pressure is often an early sign of malignant change, and several of our cases have been diagnosed correctly on the basis of this observation. Unfortunately the innocent goitre, though usually painless, is occasionally painful; a haemorrhage, for instance, can very closely simulate malignancy; and as a rule it is only in the laboratory, after operation, that early malignant change can be definitely diagnosed.

3. *Pressure.*—Displacement, distortion, and narrowing of the trachea are some of the commonest findings in the examination of patients with large goitres, particularly of the nodular type, and more especially if there be retrosternal prolongations. Sometimes no symptoms result; in some patients, however, the goitre causes definite stridor and distress—possibly only on effort—or a mild dysphagia. A persistent irritating cough, again, may occasionally be the presenting symptom, while one of the earliest symptoms of all can be a choking sensation which awakes the patient. These symptoms are all due to chronic pressure, but a nodular goitre—even a foetal adenoma in a young subject—may occasionally be the seat of a sudden haemorrhage causing pain, swelling, and frightening sensations of suffocation. Death seldom follows, though this has happened once in our clinic.

II. That to diagnose toxic goitre it is necessary to find tachycardia

There is little doubt that the cardiovascular, nervous, and metabolic systems are all affected to some degree by toxic goitre, but sometimes, for an unknown reason, only one, or it may be two, of these systems are affected to any marked degree. Thus we have seen a number of patients with many of the classic symptoms of toxic goitre in whom the heart rate is little, if at all, increased over the period of observation. In this connexion it may be worth while to add that during the intervals between attacks of paroxysmal auricular fibrillation due to toxic goitre the heart rate may be normal or rarely slower than normal.

III. That loss of weight is a constant feature of toxic goitre

This again is not true. Maintenance, or even an increase, of weight is not very uncommon even in patients with primary toxic goitre, where loss of weight is a recognized cardinal symptom. As was pointed out in the previous section, the toxic process may miss, or almost miss, the metabolic system, and this may be the cause of the phenomenon. Sometimes a ravenous appetite, combined with a good digestion and efficient absorption, may in its effects counterbalance or even exceed—for a time at any rate—those produced by an increased metabolism. But doubtless there are other reasons, at present unknown to us. It has, by the way, been urged by Trotter and Eden (1941) that surgical treatment in plump patients with Graves's disease is attended with a greater risk to life and is less satisfactory than in the ordinary type of patient. This is not confirmed by our experience.

IV. That no goitre should be considered toxic unless the basal metabolic rate is found to be above normal

This would seem to be almost an article of faith among the profession as a whole, and perusal of the recent spate of papers on thiouracil has done nothing to weaken our impression.

Regarding the test, the late Cecil Joll was wont to say in his later years that, though it was the best laboratory test we had, it was "a poor best"; and with this opinion we fully agree. A test which accounts readings of 15 points above and below normal as "within normal limits" can hardly be regarded as satisfactory, and the fact that the same patient under apparently identical conditions can give very different readings on two successive days shows how misleading single estimations may prove. We fully appreciate the far greater value of a "level" based on a large number of estimations made at short intervals; but, unfortunately, in this country the necessary finances and facilities are generally lacking. Again, even in definite thyrotoxicosis, exacerbations and remissions are, as we have already said, comparatively common, and during a period of remission—which may be long—the basal metabolic rate may be within normal limits. The point, however, which we especially wish to make is that in the very large and important group of goitres to which we have drawn attention, where the toxicosis is minimal and yet the danger of eventual auricular fibrillation is real, so little is the general metabolism affected as a rule that it is rare to find the basal metabolic rate significantly raised.

We have no desire to decry the occasional value of the test, but the longer our experience has become the greater emphasis we have tended to put on an appraisement based on a careful clinical examination. That a course of thiouracil in doubtful cases might provide valuable evidence for or against the presence of thyrotoxicosis occurred to us, as to others, soon after its introduction, and we have often used it for this purpose. It is as yet too early to speak definitely, but such a therapeutic test may possibly prove an adequate substitute for an estimation of the basal metabolic rate.

V. That iodine cures

We rarely see a new patient with toxic goitre who has not been taking iodine for weeks, months, or even years. There is no evidence whatever for the belief that this drug cures. Waller (1914), in the original paper on its use in Graves's disease published in the *Prescriber*, did not make this claim; nor has any authority done so since. Its beneficial results are, unfortunately, only temporary, and its use ought, in our opinion, to be restricted to the period immediately preceding, and possibly that immediately following, operation. It is doubtful indeed if, owing to its misuse, it has not been more of a curse than a blessing in the treatment of thyrotoxicosis. Through the widespread belief in its curative power operation has often been unduly delayed until heart complications, extreme emaciation, or even a psychosis have supervened.

VI. That treatment by deep x rays is a satisfactory alternative to surgery in toxic goitre

This belief is probably not so widespread as it once was, but it still persists. This little we would say on the subject: *x*-ray therapy is generally conceded to be of no value in nodular toxic goitre—and in this connexion it is well to realize that many goitres, which clinically do not appear to be nodular, are found at operation to be of this type. Furthermore, as regards primary toxic goitre, Joll, who was extremely doubtful of the value of *x*-ray therapy, used to say that the radiologists who wrote so strongly in its favour seemed to forget that a large part of the gland was situated behind the trachea, so that irradiation powerful enough to destroy gland tissue in such a situation would almost certainly cause serious damage to the tracheal mucous membrane. In any event the results have, in our own experience, for the most part proved very disappointing. One of the most devastating criticisms of this mode of therapy was made by Dunhill (1935), an erstwhile member of our unit, when he stated that of 140 adults so "cured" no fewer than 118 were found to have established auricular fibrillation at a later date. In face of such a statement it would seem unnecessary to pursue the argument further.

VII. That the advent of thiouracil has removed the need for operation save to relieve pressure symptoms or for cosmetic reasons

This doctrine is being widely preached at the present time, and enthusiastic reports of the virtues of the new drug follow one another in the journals with an almost monotonous regularity. Even the writer of a leading article in the *Lancet* of April 14, 1945, declared, with regard to the question whether thiouracil should replace thyroidectomy as the standard treatment of toxic goitre, that there were strong indications that it might do so. From the first, voices have been raised protesting that the claims made for it are excessive and that various

dangers attend its administration, but they have tended to be drowned in the chorus of approval. We soon felt it our duty to add our voices to those of the minority. To us it was deplorable that a drug, potent not only for good but also for evil, should be thrown on the market to be used indiscriminately and generally speaking without adequate supervision, until much more was known about the indications for its use, its limitations, and its dangers. That by preventing the final synthesis of thyroxine in the gland it can in most instances inhibit thyroid activity and so alleviate thyrotoxic symptoms, there is no doubt; that in patients in whom the toxicosis is temporary and self-limited it can maintain normal health till the attack is over appears likely; that already numbers of patients have been able to resume and maintain their normal activities as long as the treatment is continued, and that in a considerable proportion remissions can last for many months after a discontinuance of the treatment, is certain; but up to date there is no convincing evidence that it cures.

As matters stand it would seem that for its beneficial effects to be maintained it must usually be given for an indefinite period, since thyrotoxic manifestations almost always recur sooner or later after its discontinuance, and generally sooner. Furthermore, as Grainger, Gregson, and Pemberton (1945) point out, initial improvement is sometimes followed by relapse while the patient is still under treatment. Nor must it be forgotten that some patients prove recalcitrant, and that in 10 to 20% of those treated there are complications—some merely annoying, others frankly dangerous. This should soon damp the first enthusiasm, especially as the possible complications are many, and it would appear that their number grows with the growth of experience of the drug. Headache, nausea, and vomiting—usually transient, but occasionally so severe or prolonged as to cause discontinuance of the treatment—pyrexia, splenic enlargement, various rashes, adenitis, enlargement of the salivary glands, diarrhoea, jaundice, oedema, pains in the joints, leucopenia, thrombocytopenia, agranulocytosis, and myxoedema are some though not all of those which have been described. Of these a certain degree of leucopenia is usual, and in the large majority of patients has no serious import. Agranulocytosis is, however, in a different category, since it carries a high mortality. According to the latest American statistics it has occurred in over 2% of the patients treated whose records are available, and it is now known that it may develop with disconcerting suddenness, which is not necessarily dependent on the dosage and may not be presaged by a notable fall in white cells. As Cookson (1945) has pointed out, a long period of perfect tolerance to the drug may end in this or some other toxic reaction. It is argued that comparatively few deaths due to thiouracil have been reported to date, but with its wide use among practitioners, many of whom are unlikely to be able to make the difficult diagnosis of agranulocytosis, the number of deaths from this cause alone is almost certainly greater than that recorded, and, furthermore, we would suggest that a drug proved capable of causing severe damage not only to the haemopoietic system but also to the liver in certain patients treated for a short time is not unlikely to cause harm to all patients treated for a long time; and the warning given by Broders and Parkhill (1944) that "the thiouracil goitre is more of a cellular hyperplasia with mitosis very much in evidence and so, therefore, more comparable to a carcinoma," only adds to our apprehension. As to the effects of thiouracil on the size of the goitre, although many examples of primary toxic goitre have been described in which after long treatment there has been a marked decrease in size, occasionally the tendency is to an increase which, in our experience, may be amazingly rapid. Little, if any, decrease can be expected, of course, in nodular toxic goitres.

All this, however, is not to say that there is no place for thiouracil in treatment. From the first we have held with Lahey (1945) that it has a very valuable use in preparation for safer operation, if not as a method of cure; and now the conclusions reached by the American Council of Pharmacy and Chemistry (1946), based, as they are, on a survey of no fewer than 5,745 patients treated with it for various periods, would appear to prove us right. They are that available evidence shows that thiouracil can be recommended only in pre-operative treatment and where operation is for any reason contraindicated. Before the publication of this report, however, we had formed the opinion that surgery in good hands is greatly superior to thiouracil as a mode of treatment. It offers a prospect not only of rapid removal once and for all of the tumour and the manifest dangers connected with its presence, such as pressure, haemorrhage into its substance, carcinomatous change, and the not unimportant anxiety the mere presence of a tumour occasions, but also of a rapid disappearance of thyrotoxic symptoms. The risk of development of auricular fibrillation is practically removed, and where it is present there is good hope of a quick return to normal rhythm. Convalescence too is relatively brief. In addition we believe that in the end the mortality rate will be found to be lower.

VIII. That patients with auricular fibrillation and gross signs of congestive failure are too ill for operation

This, we find, is a fairly common belief in the profession. Yet we have seen scores of such patients not only come safely through the operation (sometimes done in stages) but even take on a new lease of active life and enjoy reasonable health for years afterwards. Admittedly the operative risk is greatest among these patients, but several who were apparently moribund have been saved. If, and only if, a marked degree of thyrotoxicosis is present is thiouracil indicated in the preparation of this class of patient, so far as our experience goes. Then it may prove to be of the greatest value.

IX. That the results of subtotal thyroidectomy in toxic goitre are usually unsatisfactory

Had we not heard this opinion of the value of the operation expressed on several occasions by postgraduate students we should not have deemed it worthy of inclusion in our list. We can only think that these observers have been unfortunate. The operation is regarded by thyroid surgeons everywhere as one of the most satisfactory. Dunhill (1934), for instance, found that 84% of 428 patients were able to live "approximately normal lives" after operation; Joll (1932) that 90% were able to return to a "full and active life" within three months of operation; and Keynes (1935) that nearly all patients operated on were enabled to live an approximately normal, instead of a semi-invalid, life, and the majority to assume full activity both physical and mental.

Nursing is generally recognized as one of the most arduous professions, and yet of some 50 nurses operated on for toxic goitre at our clinic all have resumed full work. As regards cardiac complications, one can almost promise subjects of paroxysmal auricular fibrillation that they will lose their attacks altogether after operation, while the majority of those with established auricular fibrillation regain normal rhythm either spontaneously or with quinidine, and in those who fail to do so the ventricular rate can nearly always be adequately controlled by digitalis. At the same time it must be emphasized that in patients with long-continued auricular fibrillation, and especially in those in whom congestive failure has resulted, the heart is irretrievably harmed to a greater or less degree, and expectation of life is consequently shortened. Generally speaking, auricular fibrillation, even paroxysmal, is an indication that surgery should have been brought to bear at an earlier stage.

X. That subtotal thyroidectomy in goitre, and especially in toxic goitre, is such a dangerous operation that it should be advised only as a last resort

That it carried a very high mortality up to twenty-five years ago is true. That to-day in uninstructed and inexperienced hands the mortality rate is too high we agree. In the hands of the expert surgeon, and especially if he is a member of a trained team, it is a very different matter. In such circumstances the figures show a mortality rate for all goitres operated on of considerably less than 1%, and for toxic goitres of approximately 1%, whether they come from clinics in America, Australia, New Zealand, or this country. As this paper is written primarily for readers in this country it may interest them to know that our figures compare favourably with those of the best clinics abroad; for instance, one of us (G.K.) has operated on some 3,700 goitres—mostly toxic—with a mortality

rate of less than 1%, and another (J. E. P.) has had but one death in his last 360 cases. By the judicious use of thiouracil it is now possible, in patients with the most profound thyrotoxicosis, to achieve a degree of pre-operative improvement which was previously beyond the capacity of iodine treatment. Thus not only will stage operations, formerly sometimes necessary, usually be avoided, but the mortality rate will be almost certainly still further reduced, so that an operative death should be a very rare event. It is, however, to be remembered that the gland substance, after treatment with thiouracil, is intensely vascular and friable, with the result that operation becomes a most difficult and trying business. The vascularity can, however, be greatly reduced by discontinuing the thiouracil for two or three weeks before operation and substituting iodine—a procedure which we believe we owe to Bartels (1945) of the Lahey Clinic.

XI. That thyroid surgery requires no apprenticeship, and that the results of the occasional thyroid surgeon compare with those of the thyroid unit

Though few technical difficulties are likely to be encountered in many uncomplicated goitre operations, yet there is an important minority where such difficulties are very real, extending even the experienced thyroid surgeon to the utmost. Again, no two goitres are alike, and therefore, contrary to the usual belief, there can be no uniformity as regards the general surgical procedure. In addition the medical, in particular the cardiological, side is a matter of the greatest importance, and demands that the surgeon be associated with a physician with special qualifications. Also, in no other branch of surgery is there a greater need for an experienced anaesthetist, ether anaesthesia being, in our opinion, almost entirely contraindicated. Finally, the nursing staff not only should be experienced in dealing with the many difficulties and dangers that may arise before and after operation, but should be possessed of sympathy, consideration, and ability to inspire their charges with the greatest possible confidence. We realize that the ideal is often unattainable and that all goitres cannot be treated at goitre clinics; at the same time, it should be within the capacity of most surgeons interested in goitre surgery to organize teams on the lines we have indicated. We are convinced through our own experience that they will find it well worth their while.

Conclusion

There are, of course, many other fallacies we could discuss, but those we have dealt with are in our experience some of the most important.

In concluding we would ask a question, which is also being asked again and again by thyroid surgeons to-day in America. It is this: In face of the many dangers which beset it, ought not at any rate every nodular goitre to be removed surgically without undue delay? It was a favourite saying of Joll's that no doctor in his senses waits for a tumour of the breast to develop secondaries before he advises operation, and so why should one wait for auricular fibrillation, pressure symptoms, carcinomatous change, etc., to develop in a patient with a goitre before one advises operation?

REFERENCES

Bartels, E. C. (1945). *Ann. intern. Med.*, **22**, 365.
Broders, A. C., and Parkhill, E. M. (1944). *Surgery*, **16**, 633.
Cole, W. H., Slaughter, D. P., and Rossiter, L. J. (1945). *J. Amer. med. Ass.*, **127**, 883.
Cookson, H. (1945). *Lancet*, **2**, 485.
Council of Pharmacy and Chemistry (1946). *J. Amer. med. Ass.*, **130**, 343.
Dunhill, T. P. (1934). *Bristol med.-chir. J.*, **51**, 155.
—— (1935). *British Medical Journal*, **2**, 798.
Grainger, A., Gregson, D. A., and Pemberton, H. S. (1945). Ibid., **2**, 343.
Hertzler, A. E. (1936). *Surgical Pathology of the Thyroid Gland*, Lippincott, Philadelphia.
Joll, C. A. (1932). *Diseases of the Thyroid Gland*, p. 617, Heinemann, London.
Keynes, G. (1935). *Practitioner*, **135**, 743.
Lahey, F. H. (1945). *J. Amer. med. Ass.*, **127**, 887.
Linnell, J. W. (1945). *Practitioner*, **154**, 138.
Papp, C. (1945). *Post-grad. med. J.*, **21**, 45.
Trotter, W. R., and Eden, K. C. (1941). *Lancet*, **2**, 335.
Waller, H. E. (1914). *Prescriber*, **8**, 153.

Lady Florey, who has carried out much valuable research work at Central Middlesex County Hospital while holding an appointment with the Medical Research Council which is now due to terminate, has been appointed research consultant at the hospital, with an annual honorarium.

ASTHMA IN CHILDHOOD

BY

T. N. FISHER, M.B., M.R.C.P., D.P.H.

Assistant Physician, Royal Manchester Children's Hospital; Honorary Physician for Children, Manchester Northern Hospital; Consulting Physician for Children, Warrington Infirmary

The following remarks are based on the case-notes of children suffering from asthma who have attended my out-patient clinic at the Royal Manchester Children's Hospital during the last twelve years. The main object is to draw attention to an increasing lack of balance in the approach to the problem of asthma in childhood. Too much is expected from detailed investigation of the child in hospital or asthma clinic and from the use of specific and non-specific forms of protein therapy, and not enough attention is paid to the study of the child in his normal surroundings.

This paper is concerned with those general principles that have been found helpful in the long-term treatment and management of the child and his disability—principles that are mainly directed to ensuring that the child is placed under the best possible conditions, in his natural home surroundings, for combating the disease and evading the establishment of the asthma habit. It is this aspect of the disease that I have found to be most neglected, as a result either of failure to diagnose the allergic disease in its earliest stages, or of failure to recognize the leading role that the nervous system plays in the establishment and perpetuation of the disease.

Diagnosis

The importance of early correct diagnosis cannot be overemphasized. Of 200 children, 48% developed symptoms during infancy, either spontaneously or as a result of the mild physiological strain of teething. Here we have asthma in its purest form, uncomplicated by organic tissue change or mechanical chest deformity. Another 39% had their first attack between the ages of 2 and 6 years, often ushered in by some respiratory infection, with measles and whooping-cough well to the fore. A proportion of the children with this type of onset exhibit that inextricable blending of allergic and inflammatory disease known as the "lung-damage type" of asthma. In 87% of these children, therefore, asthma was manifest before the seventh year of life.

Chest symptoms of unexplained origin in early life should immediately arouse suspicion of allergic disease. Unfortunately diagnosis is further confounded by the ambiguous clinical picture that asthma presents at this age. Of the two closely associated allergic phenomena that are responsible for the asthma attack, turgid swelling of the mucous membrane of the smaller branches of the bronchial tree, with increased permeability and exudation of fluid, plays the dominant role in early childhood, gradually to be superseded by smooth-muscle spasm, with its characteristically more abrupt manifestation, as the child grows older. As a result of this, early allergic disease closely simulates inflammatory disease of the bronchi. Unless allergic disease is borne in mind, and the evidence for or against it carefully weighed in the light of the family history and of other symptoms presented by the child, a hasty and much too casual diagnosis of bronchitis is made, with its implication of inflammatory disease. This is a cardinal error, responsible for much subsequent confusion, anxiety, and misdirection of treatment. If muscle spasm plays an unusually predominant part the onset of the attack is more abrupt and the child is more acutely ill, with obvious respiratory distress which, in these thermolabile subjects, readily induces pyrexia. The clinical picture then bears a superficial resemblance to bronchopneumonia. To the discerning eye, however, the patient's distress is obviously due almost entirely to respiratory embarrassment; toxic symptoms are absent, recovery is rapid, often dramatically so (to the no small credit of whatever form of drug therapy has been employed), and the whole sequence of events is apt to recur, for no ascertainable reason, at intervals of a few months.

It may be that only at the age of 5 or 6 an acute spasmodic attack of the more adult type of asthma throws a sudden