Remarks ON BRONCHIECTASIS *

BY

CHARLES McNEIL, M.A., M.D., F.R.C.P.Ed.
PHYSICIAN, ROYAL EDINBURGH HOSPITAL FOR SICK CHILDREN

The subject of bronchiectasis is a suitable one for discussion at the Centenary Meeting of the British Medical Association, for this memorable date almost coincides with the centenary of the discovery of this condition. It was described for the first time in 1819 by Laennec in his great book *Auscultation Médiate* in a short chapter entitled "On dilatation of the bronchi."¹ Here Laennec described the morbid anatomy of four cases, and gave a brief account of the clinical history and of the physical signs during the fatal illness. For many years little was added to our knowledge of the subject, although there was much theorizing about the mechanism of bronchial dilatation.

In 1894 Clark, Hadley, and Chaplin² published a full account of forty-five cases. This was almost entirely a clinical study of living cases, as distinguished from the post-mortem study of Laennec. At this date it was now possible to separate accurately tuberculous from non-tuberculous disease of the lungs by the bacteriological examination of the sputum, so that in this large series of cases tuberculous disease as an aetiological factor in the condition was excluded. This non-tuberculous and chronic disease was termed "fibroid disease of the lung," although it was admitted that bronchiectasis was nearly always associated with the fibroid condition. Of the forty-five cases, one-half were under 15 years of age and nine under 10 years; but the clinical records showed that the symptoms of cough and spit had begun under 5 years in thirty-six of the cases.

In 1922 Sicard and Forestier³ introduced the use of lipiodol injection into the trachea in combination with radiography, and so made it possible to verify and to give an exact demonstration of bronchial dilatation. This important advance was thus made in Paris just a hundred years after Laennec's discovery of the condition: it permitted a study of the morbid anatomy of bronchiectasis in the living subject with far more precision than by any other clinical method, and it may be described as the final diagnostic test of bronchiectasis. Findlay and Graham in 1927⁴ published a study of twenty-three cases of bronchiectasis. Their communication was important in the number of the cases, in the fact that they were all in children and the condition was thus studied at a stage much nearer its commencement, in the verification of the diagnosis, and in the clinical demonstration of the different degrees and types of bronchial dilatation by lipiodol x-ray photographs.

During recent years the treatment of bronchiectasis, and, to a less extent, its diagnosis, have been approached in a new way by the perfection of the bronchoscope and by the use of bronchoscopic lavage. A variety of surgical procedures dealing with the condition by way of the pleura and lung have also been tried. There has thus been a revival of clinical study of bronchiectasis, and a trial of new methods of treatment. The moment is therefore opportune for a review of the subject.

CLINICAL FEATURES

The main outlines of the clinical picture are well defined. The condition begins in early childhood in the great majority of cases, and in most cases dates from an

acute respiratory illness—bronchitis or pneumonia. Wherever a series of cases is recorded, the frequency of measles and whooping-cough or both, as the originating acute illness, is remarkable. After recovery from the acute illness the child continues to cough; and sooner or later the cough takes on characteristic features. It is paroxysmal, occurring in periodic bouts, which generally take place as soon as the child awakens in the morning, are violent, and often end in vomiting. They also occur during the day, after some exertion or excitement. Sputum is often copious, but may be scanty; in childhood it is generally not fetid, and is green or yellow according to the amount of pus present. From time to time there may be slight streaking of blood in the sputum; free haemoptysis is uncommon in childhood, but after some years, and in certain types, free and recurrent haemoptysis may occur, as described by Laennec and Clark, and recently by Pinchin and Morlock.⁵ There may be intervals when the cough disappears entirely, but when the condition of bronchiectasis is established, this characteristic cough and expectoration are sure to return; the cough is coterminous with life.

The duration of life may be prolonged for many years, and remarkable cases of longevity are on record. The child is subject to exacerbations of this cough—acute febrile illnesses with bronchitis and pneumonia—and more often than not it survives these acute attacks. The general health, nutrition, and activity are surprisingly good, although there is a little dyspnoea. The general condition often varies with the amount of the sputum, improving and worsening as it diminishes or increases. In most cases there is some clubbing of the fingers and toes, and in nearly all, some degree of cyanosis; but extreme clubbing and cyanosis are uncommon.

The physical signs are much less constant, and much less reliable in diagnosis. They depend upon the amount of dilatation of the bronchi, upon the presence of sputum, and upon the amount of associated fibrosis of the lung tissue. The most constant sign is crepitation, persisting or recurring in the affected area; there is generally also a blowing breath sound of low pitch, and pectoriloquy in the vocal resonance. If massive fibrosis is present there will, of course, be percussion dullness; and if the pleura is thickened as well the breath sounds and their accompaniments may be scarcely audible. This feebleness of the breath sounds may also be present when the dilated bronchi are filled with secretion, and will be replaced by cavernous breathing when they are emptied by coughing. This variation in the auscultation signs in bronchiectasis is in itself significant.

The history and long course of the illness, the peculiar character of the cough and sputum, and the physical signs in the lung, together form a clinical syndrome which is unmistakable. There ought to be no difficulty in the diagnosis of bronchiectasis and in its differentiation from other clinical conditions in which cough is a prominent feature. The use of lipiodol is a further aid to diagnosis, and has given us a valid diagnostic test of bronchiectasis. More than that, in its accurate tracing of the extent and character of the bronchial dilatations it has established the existence of minor types of the condition.

DIFFERENTIAL DIAGNOSIS

Tuberculous disease of the lung in childhood, chronic bronchitis, and chronic cough produced by nasopharyngeal catarrh are all conditions in which cough is a prominent symptom, and in which there may be difficulty in diagnosis. It is very common for cases of bronchiectasis to be regarded as tuberculous; but the long benign course and the absence of bacilli from the sputum in bronchiectasis makes distinction between the two conditions an easy matter.

* Paper read in opening a discussion in the Section of Diseases of Children at the Centenary Meeting of the British Medical Association, London, 1932.

There is more difficulty with those cases of chronic cough and bronchial catarrh following measles and whooping-cough or simple acute bronchitis and bronchopneumonia. The cough may continue for years, and, in the cough and other clinical features, these cases may resemble true bronchiectasis. Agassiz and Gill⁶ have described a large number of cases which they call "non-tuberculous fibrosis of the lung." Reading their careful record, one cannot doubt that they are describing a condition closely allied in pathology and clinical features to true bronchiectasis, and probably differing from it only in degree. So far lipiodol has not been used extensively in these cases, and it is quite likely that some will, by this method, show a minor degree of bronchiectasis. These cases are much more numerous than those of definite bronchiectasis. In them, too, there is organic bronchial damage and fibrosis, although without pronounced dilatation, and it is desirable that they should be grouped alongside true bronchiectasis and regarded as closely allied conditions. In younger children these cases of fibrous bronchitis may well be the early stage in the evolution of true bronchiectases, but in many instances definite bronchial dilatation does not seem to develop. The extended use of lipiodol may, however, alter our views on this point.

Another type of case is in the convalescent stage after a severe bronchopneumonia, and especially after whooping-cough and measles, where for some weeks there may be violent paroxysmal coughing and fairly copious sputum, and where a commencing bronchiectasis may be feared. Some of these cases probably have a dilatation of the bronchi which is temporary and which, after some months, gradually but entirely passes away.

CLINICAL TYPES OF BRONCHIECTASIS

Two types may be described. Where bronchiectasis is accompanied by massive fibrosis of the lung it is entirely or predominantly unilateral. These cases are the least common, but they are most easily recognized by the ordinary clinical methods. The use of lipiodol will demonstrate with precision the pattern of the bronchial tree and the extent of mediastinal displacement. Before lipiodol was introduced these unilateral cases perhaps formed the majority, and left-sided bronchiectasis was commoner than right-sided; but they are actually less numerous than bilateral. On the whole, cases of unilateral bronchiectasis with massive fibrosis run a benign course, and are compatible with good nutrition and vigorous health: this is probably due to the collapse of the lung resulting from the fibroid contraction and to the absence of great bronchial dilatation and catarrh.

Bilateral bronchiectasis is the commoner type in childhood. Here the accompanying fibrosis of the lung is less, and the bronchial dilatations and the peribronchial fibrosis are usually confined to the bases of the lung and close to the vertebral column, so that the detection of this type by physical signs of percussion and auscultation is more difficult. Their demonstration by the use of lipiodol is very exact. The branches of the left bronchi are nearly always more affected than the right. In my own experience the more severe cases are found in this group; the cough is worse, the sputum more copious, and the general condition of the child more unsatisfactory. At the same time the degree of dilatation varies much, and in this bilateral group there are also cases where the dilatation is slight, producing a uniform slight dilatation of the main bronchial branches without terminal sacculations: in these, although cough is troublesome, sputum is scanty and the general health may remain good. These more benign cases of bilateral bronchiectasis shade off into, and are not essentially different from, the numerous cases of

chronic bronchitis with fibrous change in the bronchial walls and permanent damage, but in which no dilatation can be demonstrated by lipiodol.

FREQUENCY OF BRONCHIECTASIS

When one considers the fact that most cases of bronchiectasis are due to infection and inflammation of the bronchial tracts and lungs, and also the huge aggregate of cases of bronchitis and pneumonia in this country, true bronchiectasis is a rare sequel of these diseases. It is very difficult to give an approximate estimate of its frequency. In the last 1,000 cases of medical diseases admitted into my hospital ward there were eight cases of bronchiectasis, verified by lipiodol x-ray photographs, and in eleven years of hospital practice I have records of thirty-one cases. This series of cases includes seven post-mortem examinations, in only one of which the condition had been observed or detected in life; and in some of these it was at an early stage. Without attempting any statistical statement, it may be said that the condition, in its established form, is an uncommon one, either as a clinical disease or as a post-mortem finding.

PROGNOSIS AND COURSE

A remarkable feature of bronchiectasis is the contrast between the serious and extensive lesions in the lungs and the not unsatisfactory state of the general health. This fact is brought out in the clinical records from Laennec to the present time. The condition, even in advanced cases, is compatible not only with years of life, but with a fair degree of health and vigour and with the capacity to earn a living. Laennec's account of an old teacher of the piano, who died in his ward at l'Hôpital Necker aged 72, is the classical example of longevity in bronchiectasis. This old lady had been troubled since childhood with a cough and abundant expectoration, and with frequent haemorrhages, but she never considered herself sick and was always able to attend to her affairs. She was but a few days in hospital, and died of nothing but old age (*cassée de vieillesse*). Post-mortem examination showed extensive bronchiectasis of the right upper lobe, and to a much less extent in the left upper lobe.

It would be foolish to base prognosis upon one case. But there is also the series of forty-five cases of Clark, Hadley, and Chaplin. In these the average period of survival from the original illness was eleven years; there were but three deaths, and the great majority were "not only alive but also in the enjoyment of excellent health." But it is still possible that many of the patients may die in childhood in the early stages of the disease. Findlay and Graham⁷ have recently shown that a considerable number of patients did not survive childhood, and their view is that the general prognosis in childhood is grave. My own experience, derived from a study of thirty-one cases, many of which have been under observation for five years and more, is that most of the deaths take place within a year or two of the establishment of the condition. If the children survive this period of danger their chance of survival through the remainder of childhood is fairly good.

In my series of cases there were ten deaths; five deaths occurred at or under 2 years, and in most of these the condition was at a very early stage of development. The principal causes of death were pneumonia and empyema; indeed, of the known causes of death empyema was the commonest, and this complication also occurred in one of the non-fatal cases. Cerebral abscess did not occur in any. I have not found children with bronchiectasis to be specially susceptible to tuberculous infection, and my series of cases included several where the cutaneous tuberculin test was positive, and where, over a period of five years and more, no tuberculous disease has developed in the lungs or other parts.

Does "cure" of bronchiectasis ever take place when the condition has been established? This seems hardly likely, but cases are on record where great and apparently permanent amelioration of symptoms has occurred. Hutinel⁸ has described several examples of this kind, but is careful to add that there remained a tendency to recurrent catarrhal and coughing attacks. In the process of bronchial dilatation there is a stage of development which varies in length from a few weeks to a few months. It is in this stage that treatment might be expected, not to restore the integrity of the bronchial walls, but to prevent the further evolution of the process.

Some writers speak of a "progressive worsening of the condition" extending over years, both of the bronchial dilatation and of spread of the fibrosis. I have not seen this happen in my cases: stabilization of the process had occurred when they came under my observation, and, over periods of observation up to eleven years, there was no appreciable organic change in either the lungs or the bronchi. In one boy with extensive unilateral bronchiectasis of the right lung no physical change could be observed over a period of eleven years: he came under observation at the age of 1½.

In the acute and convalescent stages of severe bronchitis and of bronchopneumonia, and especially in whooping-cough and measles, an acute dilatation of bronchi may take place. This need not be a permanent condition if the bronchial walls are only stretched without destructive lesions in their walls. The term "bronchiectasis" should not be used to describe this temporary stretching, which is found often enough at post-mortem examination of fatal cases; it should be reserved for cases of permanent structural damage of the bronchial walls.

THE PATHOLOGICAL PROCESS IN BRONCHIECTASIS

All cases of bronchiectasis do not begin in childhood, but it is probable that the great majority do. The older clinical and post-mortem records of the condition in adolescent and adult life establish beyond doubt its commonest origin in early childhood, and they give valuable hints as to the general nature of the originating illness. Recent careful clinical studies of the condition in the child confirm these observations. In most cases this originating illness is a definite and severe attack of bronchitis and bronchopneumonia, and in all large series of cases measles and whooping-cough easily take first place, although instances of bronchiectasis following simple bronchitis and pneumonia are common enough. The characteristic and persistent cough begins soon after recovery from such an illness. In a few cases it begins more insidiously, without an antecedent definite attack of bronchitis or pneumonia, and in this much smaller group the cough may even begin in the first year of life. The aspiration of foreign bodies, of food material, of pus and blood from septic or operation areas in the throat and nose, account for a few cases, but in the aggregate they form a very small fraction of the whole. In my own series there was one case almost certainly due to the aspiration of a foreign body. I have not met with a case that followed pleurisy or empyema.

All these types of originating illness consist of, and begin with, bronchial catarrh and inflammation. It may be accepted that the largest number of cases are the sequel of acute bronchitis and bronchopneumonia, and especially when associated with measles and whooping-cough. But it is a curious and striking fact that, although these diseases in their severest forms are very numerous in hospital practice and under close observation, bronchiectasis is seldom detected there in its earliest stage. The symptoms of the condition thus do not seem to start "at full blast": there appears to be a stage of evolution when the characteristic violent periodic cough and sputum are not

developed, although the pathological condition of bronchiectasis may already be present.

Although bronchiectasis is seldom discovered clinically in its earliest stage, there are occasional opportunities of studying the pathological process in early fatal cases. With my colleagues Dr. Agnes Macgregor and Dr. W. A. Alexander⁹ I have examined five early fatal cases. In all of them the primary change was ulceration, suppuration, and complete destruction of the original bronchial walls, then the replacement of these walls by organizing granulation tissue and by a cubical and non-ciliated epithelium; in these areas the lumina of the bronchi were converted into irregular spaces, and bronchiectasis was already present. Adjoining these destroyed and reconstituted bronchial walls young fibrous tissue was infiltrating the lung.

These findings have a bearing on the old controversy as to the mechanism of bronchiectasis. They give no support to Corrigan's theory, still widely held, that bronchiectasis is produced by traction upon the bronchial walls by fibroid change in the lung itself. They show that the primary change in early bronchiectasis as seen post mortem is an intense inflammation of the bronchi which destroys their walls. Before death these cases showed the symptoms of troublesome cough and sputum, but not the characteristic cough and copious sputum of bronchiectasis. It is easy to imagine what the further developments would have been. These re-formed and weak bronchial walls had lost their ciliated epithelium, their muscular coats, and their cartilages. Secretions would accumulate within them, and, in coughing, would be expelled with difficulty, and would further distend the weakened walls. Sooner or later the clinical features would emerge. But in this pathological process fibrosis of the lung would seem to play only a minor part.

In this group of fatal cases showing bronchiectasis in its early stage of evolution the primary pathological process was shown to be a suppurative and ulcerative bronchitis, which destroyed the bronchial walls. This seems to indicate that in all cases of bronchiectasis which begin with bronchitis the primary and essential change is in the bronchial wall, either an acute destructive inflammation or a more chronic weakening and disintegration.

TREATMENT

In bronchiectasis we are dealing with several morbid conditions—bronchial catarrh, the retention of secretions in the bronchial dilatations, and fibroid change in the bronchi and adjoining lungs. The fibroid change is an incurable condition, but it is also rather a help than a hindrance in limiting bronchial dilatation.

In our treatment we cannot hope to do more than reduce the size of the cavities and procure a regular emptying of their contents; in actual practice we can seldom achieve so much. These two objects may be attempted by medical and hygienic measures alone, or by adding to them more radical and surgical procedures. I hope that the discussion will draw out information regarding a variety of recent radical procedures. So far the medical treatment of bronchiectasis must be described as ineffective. In most cases it has only achieved an amelioration of the symptoms, and its comparative failure has encouraged and justified the trial of bolder measures.

Of medical measures the most effective is daily postural drainage, the child lying on its face on a steep inclined plane for at least half an hour once or twice a day, and continuing to do so until there is marked reduction in the quantity of sputum. I have also obtained some help from regular spraying of the nose and throat with glycerin solutions; this aids expectoration and prevents the reinfection of the bronchial surfaces from infected nasal and throat

secretions. Among the expectorants, belladonna and potassium iodide sometimes help a little. Inhalations may also help in aiding expectoration, but in my experience have not done more than that. Vaccines have been quite ineffective in my hands. In addition, the institution of good hygiene, open-air conditions, prolonged rest, and simple respiratory and gymnastic exercises are of real value in promoting good nutrition, and in maintaining the general health at a high level. Most cases of bronchiectasis respond quickly to such measures in hospital; weight increases, while cough and sputum greatly diminish. When, however, the child returns home the symptoms soon reappear. It is probable that better results could be obtained by far more prolonged treatment on the above lines, especially if such treatment could be begun and continued at an early stage in the bronchiectatic condition.

So far the published results of bronchoscopic lavage and of the great variety of chirological treatments by way of the pleura and lung are not encouraging. The more drastic procedures which extirpate the affected area of lung are attended with a high mortality. Those that aim at producing collapse of one lung are confined to the unilateral cases, which are often of benign type with a fair standard of general health and a good enough expectation of life, and in which the existing fibroid change makes further collapse difficult to attain. Bronchoscopic lavage is a safer and a more radical treatment; it is a direct attack on the real therapeutic problem of the dilated bronchi and their retained and septic contents. Its immediate results in older cases are often very good indeed, but there are difficulties in the frequent use of the bronchoscope in young children. We may hope that with improvement in the technique of the bronchoscope a real advance in the treatment of bronchiectasis will be achieved.

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RECENT RESEARCH ON THE SEX HORMONES AND THEIR CYCLICAL PRODUCTION*

BY

F. H. A. MARSHALL, Sc.D., F.R.S.

READER IN AGRICULTURAL PHYSIOLOGY AND DIRECTOR OF THE
INSTITUTE OF ANIMAL NUTRITION, UNIVERSITY OF CAMBRIDGE

The gonads differ from the other endocrine organs (with the possible exception of the pituitary) in that their functional activities are cyclical. With such glands as the suprarenal and the thyroid the same chemical substances (adrenaline or thyroxine) are produced continuously or at any rate without any marked periodicity dependent upon inherent or seasonal rhythm, but with the testes and ovaries the hormones secreted vary in character or amount with the different phases of sexual activity. This fact has often been lost sight of in seeking to apply endocrine therapy to cases of abnormality of sexual or reproductive function, and has led to the use of extracts obtained from the sexual glands in cases which are entirely inappropriate for the treatment employed.

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THE TESTICULAR HORMONE

So far as is known there is only one testicular hormone which in the lower vertebrates is presumably elaborated in amounts varying with the degree of sexual activity. In the domestic animals, most of whose males are able to breed all or nearly all the year, the hormone must supposedly be produced at all times, and for the purpose of preparing an active extract it is immaterial at what season the testes are obtained, provided that they are sufficiently developed. Moreover, there is a well-founded presumption that the testicular hormone is elaborated from the embryonic phase onwards, and that it is responsible for the development of the secondary male characters. The hormone, which is now called "provion," has recently been obtained in crystalline forms as an oxyketone with the empirical formula $C_{16}H_{26}O_2$ (Butenandt, Schoeller, etc.). Its strength has been standardized according to its potency in promoting comb growth in castrated fowls. Its use is indicated in cases of known testicular deficiency, such as bilateral orchidectomy, and possibly also in cases of senility (whether premature or otherwise) and cryptorchism associated with arrested sexual development. In assuming the existence of provion, physiologists are now on firm ground, and it is only a matter of time to establish its importance in appropriate cases of testicular deficiency.

ENDOCRINE FUNCTIONS OF OVARY

In dealing with the endocrine functions of the ovaries the matter is complicated by the fact that these organs elaborate two or possibly three or more hormones, which vary in amount at different stages of the oestrous or sexual cycle. There is probably a hormone produced from the embryonic period onwards which is responsible for the growth of the female characters and possibly also for their maintenance from puberty until the menopause. This, however, is still problematical. It is, nevertheless, certain that the ovary produces a secretion responsible for the induction of "heat" (pro-oestrus and oestrus), and another which is an essential factor for promoting and maintaining the raised uterine nutrition and associated changes in the sexual organs during pregnancy and at certain comparable periods in the absence of pregnancy.

In order to understand the parts played by these hormones and their relation to the changes which take place periodically in the different phases of the sexual cycle, it is desirable to make a comparative study of the homology of these changes in different types of mammals. The want of such study in the past has led to strangely contradictory conclusions expressed with considerable degrees of dogmatism on the part of writers of textbooks as well as of actual investigators who have limited their studies to man or to a particular group of animals. Thus, taking two textbooks of physiology in constant use among students, we read in one that the oestrus-inducing hormone when injected into women has been shown to induce menstruation (a statement which when it was made was at any rate premature), and in another the completely contradictory statement that this hormone did not induce menstruation, and that "it was unlikely it ever would." It need hardly be added that these two statements are based on contrary views as to the nature of the menstrual process and its homologues in the lower animals. So also we find Fraenkel identifying the ovarian hormone with the secretion produced by the corpus luteum, which he regarded as the ovarian endocrine organ *par excellence*, that was always present though reappearing at different times in different positions; and on the other hand Edgar Allen apparently holding the view that the secretion formed by the follicle was the same as the ovarian internal secretion. Instances of this sort of contradictory conclusion might be multiplied many times. That they have