THE ETIOLOGY OF SCOLIOSIS

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Twenty years ago the late John Cobb first showed me that scoliosis could be interesting. By the very simplicity of his teaching he changed an obscure, incomprehensible deformity into a disease which has fascinated me ever since. I recall gratefully his ability to make the complex simple.

I propose to look at this deformity in all its forms, to name the questions one must ask and answer if its etiology is to be established. At the end of this you will not know the etiology of scoliosis, for I do not myself, but it is my hope that you will comprehend the problem better.

Although idiopathic scoliosis because of its frequency, its severity and the mystery of its origin is the main problem, it is important to look at scoliosis from all causes. Scoliosis is a deformity that may be caused by many diseases, and though in some the mechanism may be clear—as for example in congenital scoliosis—in most it is wholly beyond our understanding.

After poliomyelitis, limb deformity occurs in children left with muscle imbalance while still growing; trunk muscle imbalance likewise causes paralytic scoliosis. Knowing this has singularly failed to help us to understand idiopathic scoliosis; children with idiopathic curves do not have muscle imbalance. Although there are differences between paralytic and idiopathic curves, the more remarkable feature is their similarity despite the dissimilarity of cause. It has been argued that unrecognised poliomyelitis is the cause of idiopathic scoliosis. It is now unnecessary to discuss all the reasons against this hypothesis because since the introduction of vaccine poliomyelitis has disappeared but idiopathic scoliosis has not.

Cerebral palsy, the muscular dystrophies, arthrogryposis multiplex congenita: these muscular conditions cause scoliosis and perhaps they do so by the unequal pull of unequal muscles.

Congenital scoliosis probably arises from asymmetrical growth in the abnormal vertebrae and growth plates. This seems evident, but as one cannot see the growth plates by radiography it is not known whether abnormal bone growth does cause these curves. Why is it that when one hemivertebra is present and causes a curve this rarely increases? Mechanically, once a curve is present it ought to increase. What happens to the growing areas on the concavity under pressure and those on the convexity released from pressure? It is a situation where our hypothesis suggests that the curve should always increase but observation proves that it does not.

What of the neuropathies accompanied by scoliosis? Do we comprehend the mechanisms of these curves? In the general problem of why a curve develops in syringomyelia, Friedreich’s ataxia or neurofibromatosis, not one single clue as to why deformity occurs is known. In neurofibromatosis 10 per cent of patients acquire a curve; although it is variable, there is a classical pattern (Fig. 1). Another characteristic is the acute angle at which the vertebral borders meet (Fig. 2). What is it that causes the deformity? It is not neurofibromata in relation to the vertebrae. Is it related to the disappearing bones of this disease? The vertebrae do not disappear; why indeed do bones disappear in this inherited, protean oddity? Of the scolioses due to known diseases it seems that a study of this particular condition, if it could explain how it gives rise to curves, would be invaluable in our understanding of idiopathic scoliosis. There is not yet even a working hypothesis.

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Neurofibromatosis with scoliosis. This child showed typical café-au-lait patches (skin neurofibromata seem rare in children with Von Recklinghausen's disease and scoliosis). The short, tight curve in the thoracic region is typical but there are many patterns of curve in this disease.

Marfan's syndrome and homocystinuria, both genetically determined diseases, the first an abnormality of structural protein, the latter an enzyme disorder, offer exciting links with idiopathic scoliosis. They have not, however, the same curvature, and scoliosis in Marfan's syndrome is characteristically an irregular severe double curve, a pattern not seen in idiopathic scoliosis. The associated anomalies of Marfan's syndrome, such as lens dislocation, aortic aneurysm, joint laxity and contractures, are unknown in idiopathic scoliosis. Abnormal metabolism is present in Marfan's syndrome and homocystinuria, but how does it cause the deformity?

Ponseti and Shepard (1954) elucidated the changes that induce a Marfan-like disease after giving amino-nitriles. The relationship of these experimental curves to human disease remains obscure, and perhaps there is none. Ponseti's more recent work (1968; Ponseti, Pedrini-Mille and Pedrini 1970) showed a mucopolysaccharide abnormality in the iliac apophysial cartilage of girls with scoliosis. If it were possible to obtain spinal apophysial cartilage and it showed the same abnormality it would be of great interest.
This has been, therefore, a review of some of the numerous diseases which cause scoliosis though nothing is known of their manner of producing it. Each known etiology has its characteristic curves and site of curvature, so that anyone familiar with scoliosis can make an intelligent guess about etiology from the radiograph. It is remarkable that each etiology should so specifically, so characteristically produce its own type of deformed spine. All this reminds us that we will in due course have to explain all these manifestations of spinal deformity and that any one of them may provide the vital clue in unlocking the riddle of idiopathic scoliosis.

Before turning to idiopathic scoliosis I wish to review experimental scoliosis, though only briefly, because it has added little to our knowledge. Many workers have attempted to cause experimental scoliosis and many have failed. In recent years success has been more frequent. It has been an extraordinarily difficult deformity to induce in animals. Although natural scoliosis is rare it is not unknown in mice, chickens and fish.

Methods of producing experimental scoliosis were reviewed, then repeated or initiated by Langenskiöld and Michelsson (1961, 1962) in a logical attempt to alter all the structures that might be involved: the vertebrae and ribs, the ligaments and muscles. All possible modes were worked out and the experimental procedures performed in rabbits. Curvature not unlike human idiopathic scoliosis was induced. Of the many structures that they altered, division of the costo-transverse ligaments was the only procedure that caused scoliosis consistently. Can weakness, absence, or undue elasticity of such a single, small ligament be the cause or even related to the deformity in humans? It seems unlikely. In no instance does it seem possible to relate the experimental procedure to anything that may happen to the adolescent or infant.

![Graph showing ages of onset of idiopathic scoliosis in 180 Edinburgh children.](image)

**Fig. 3**


Let us now look at idiopathic scoliosis and see what are the observed facts, what are the things that one has to explain by any etiology and mechanism. It is a curious disease: there is nothing quite comparable in orthopaedic surgery. Few of us even have a hypothesis of causation. I certainly have not, though I have been observing this disease for twenty years and must have seen some 2,000 cases.
Idiopathic scoliosis is a deformity of growing children of all ages and both sexes. In America you are particularly familiar with the adolescent girl with right-sided thoracic scoliosis, but in Europe the age distribution at onset is different. Our scoliosis clinics differ from yours and infants are almost as common as adolescents. There are two peaks in the age of onset, in infancy and adolescence, the ages of seven to eight being the least susceptible (Fig. 3). Perhaps the onset is related to the peak periods of growth.

There are a number of curious features. In the adolescent, eight girls are affected to one boy, whereas in the infant six boys are affected to every four girls, although the deformity seems identical at both ages. Equally difficult to explain is the curious change in side of the convexity of the curve. The typical infant with idiopathic scoliosis has a left-sided curve, as do 90 per cent, whereas in the adolescent 90 per cent of curves are convex to the right. In the ages of three to ten, as curves occur there is a shift from left-sided curves to a preponderance of right curves as the age of onset approaches ten. This changing of side is a feature of thoracic curves. It is conceivable that the liver of the infant pushes the spine over; if so, in 10 per cent it goes the wrong way. What causes nearly all curves to go to the right in adolescence? In the infant with double primary curves the thoracic curve is to the left, the lumbar to the right; in the adolescent with two primary curves the reverse is the case.

Idiopathic scoliosis, despite a belief that it occurs in the knock-kneed, flat-footed, bad postured child, occurs with great frequency in the husky, vigorous young girl aged ten to twelve years. Though the child is well, the progression of this deformity can be truly astonishing and alarming (Fig. 4). Nothing has mystified me more than to see a young girl in all the vigour of her youth become rapidly deformed and crippled. In few things in medicine has one so little idea of what is causing the event.
Once started, scoliosis tends to increase while growth continues. This is not surprising; Heuter's (1862) law and the work of those interested in the mechanics of rib rotation make it easy to understand why it should continue. But it does not always continue and it may stay for years unchanged.

In infants progression of the curves is quite different and of great interest. Among many hundreds of children with an onset after three years of age only twice has a structural curve been seen to disappear spontaneously; yet in infants 90 per cent of idiopathic structural curves appearing in the first year disappear spontaneously (Lloyd-Roberts and Pilcher 1965). These curves initially have fixed rotation, they persist on forward flexion or traction and yet within a few years the deformity has gone. Seemingly identical curves may progress rapidly and horribly.

If one could know what it is that allows structural scoliosis to disappear one could perhaps understand what causes it to appear. It does seem that the resolution of these curves is one of the few leads to etiology, one of the few points of attack that is offered to us. An intensive study of the difference between the progressive and the resolving idiopathic curve may one day lead to enlightenment. As in so many conditions the answer to scoliosis will almost certainly be simple and obvious—with hindsight.

The most classical form of idiopathic scoliosis is in the adolescent girl. It seems possible that significant changes in bone or ligament formation could occur from the very remarkable changes in this endocrinologically active period of life. The endocrines concerned—oestrone, oestradiol, oestriol and progesterone—are all capable of affecting bone and ligament formation. Do they act abnormally in pubertal girls with scoliosis? Are their endocrine excretions normal? These seem important questions to answer. In Edinburgh Dr M. H. Young has started collecting urine from girls who develop scoliosis just before puberty, over a three-month period each year, to determine endocrine excretion. This study is based on a detailed knowledge of the normal endocrine excretion of the pubertal girl assayed by the Medical Research Council Endocrine Unit in Edinburgh within the last few years (Loraine 1969). With such an excellent knowledge of the normal it will be possible to detect significant variations in these girls. Here is one more search for an etiology, probably to prove negative, but one facet which must be looked at in any systematic study.

The most fruitful investigations we have been able to undertake with some positive findings concern the hereditary basis of idiopathic scoliosis. From time to time clinically significant family histories are discovered. One mother with idiopathic scoliosis with three daughters, each with scoliosis, each of a different pattern, came to see me some years ago. At Wilmington Cowell, Hall and MacEwen (1969) have found some interesting families which are also suggestive.

The Orthopaedic Genetic Group at Edinburgh has made extensive and systematic enquiries into the role of heredity in idiopathic scoliosis (Wynne-Davies 1968). The technique has been to take a group of patients, 114 in this series, diagnosed as having idiopathic scoliosis. The parents and siblings, the first degree relatives, are seen in their homes and examined with their backs exposed, bending forward. If a structural scoliosis exists the patient is brought to hospital and complete examination including radiography is undertaken to confirm a true and idiopathic scoliosis. From the parents a knowledge of the whereabouts of all second and third degree relatives is sought. In all, 2,000 people have been examined, from all over Britain.

After assessment of the families the population incidence must also be discovered. In Edinburgh, examination of almost 11,000 children from infancy to eighteen years showed the incidence to be as seen in Table I. The incidence of idiopathic scoliosis of adolescent girls is nearly four per 1,000, a very considerable number.

The findings were that idiopathic scoliosis in the infant and the adolescent, clinically differing in a number of ways, seem genetically to be the same, because both occur in the same families. Overall, the incidence of idiopathic scoliosis in the families of adolescent girls affected
was twenty times that in the general population, much the same as Wynne-Davies found in her studies of club foot. Inescapably it seems that there is a hereditary factor in idiopathic scoliosis (Fig. 5), though environment and a possible polygenic mode of inheritance make the picture less clear to those used to dominant and recessive diseases inherited according to Mendelian laws. Human genetic problems are seldom simple.

An extraordinary feature of infantile idiopathic scoliosis is its rarity in North America, its frequency in Europe. In Britain a large number of babies with structural idiopathic curves are seen; they exist in the United States of America, but they are uncommon. With the evidence that idiopathic curves in infants and adolescents occur in the same families as though one condition, it is difficult to explain the absence of infantile scoliosis in North America; the genes came from Europe.

TABLE I

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<thead>
<tr>
<th>Population Incidence of Idiopathic Scoliosis per 1,000</th>
<th>(10,873 Edinburgh children)</th>
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<tbody>
<tr>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td>Early onset group</td>
<td>0.6</td>
</tr>
<tr>
<td>Late onset group</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Figure 5—The incidence of idiopathic scoliosis in the families of adolescent girls. Not only does this histogram show the marked increase compared to the general population but it also shows the halving between the first and second, second and third generations, so typical of inherited diseases. (From Wynne-Davies, R. (1968): Journal of Bone and Joint Surgery, 50-B, 24.) Figure 6—Histogram to show the increased frequency of idiopathic scoliosis in children born to mothers over 30 years of age compared to the general population (vertical hatching). (From Wynne-Davies, R. (1968): Journal of Bone and Joint Surgery, 50-B, 24.)
A significant but unexpected finding in these studies has been the increased age of the mothers of the adolescent children compared to the average age of mothers in the population (Fig. 6).

One of the most unexpected discoveries has been the association of mental deficiency (Wynne-Davies 1968). It is common to find mental deficiency in patients with scoliosis; many of us are familiar with this and its very difficult practical problems. In this series it is about seven times the incidence in the population. In the past, one has hesitated to classify curves in the mentally deficient as idiopathic in case there was an undiscovered neurological basis for the deformity.

In recent months 700 mentally deficient patients from a hospital near Edinburgh have been examined by Miss Wynne-Davies, R. L. Hay and myself. The findings were interesting though they are not yet complete. Amongst 250 mentally deficient males we have found 5 per cent with probable idiopathic scoliosis. This is over 100 times the incidence of scoliosis for men in the general population. Females with a clinical curve comprised 9 per cent, and 5 per cent had apparent idiopathic scoliosis. What this means we do not yet know, indeed it is difficult to imagine, but significant it surely must be. It is to be said that some of these curves, fulfilling the criteria for idiopathic scoliosis, are not typical and may be wrongly included (Fig. 7).

In the infantile form the evidence for inheritance, though undoubted, is less clear. Environment, particularly ante-natal and peri-natal, may be important. It is time to consider the possible role of uterine environment in infantile idiopathic scoliosis. Sir Denis Browne (1956, 1965) was always a vehement champion of intra-uterine posture as the cause of infantile idiopathic scoliosis. Congenital postural scoliosis he meaningfully called it. Congenital club foot is the orthopaedic deformity in which intra-uterine posture may most likely have a role; deformity is at its most marked at birth. In infantile idiopathic scoliosis only 5 per cent are known by the parents to have a curve at birth; the others develop it later. It seems unlikely that a baby could be born straight and later develop a curve because of its previous position in utero. Denis Browne claimed that if the newborn were examined, flexibility of the spine would be found limited in one direction and later a curve convex to this side would develop. R. L. Hay of this department therefore examined over 400 newborn babies in Edinburgh. He developed a simple device to measure flexibility (Fig. 8). Although the infants varied in their flexibility from one side to the other, sometimes markedly, such asymmetry could not be correlated with any intra-uterine or postural influences such as the duration of labour, breech presentation or multiple birth.

Plagiocephaly (Fig. 9), difficult to reproduce in a two-plane photograph but often a quite
remarkable facial and cranial distortion, is present in all babies with infantile idiopathic scoliosis even though resolving later. In normal infants of a few weeks to two years old Wynne-Davies (1968) found 10 per cent with plagiocephaly. It had always seemed to me that this facial and cranial distortion, always on the side of the curve, could indeed be explained by

![Figure 9](image-url)

**FIG. 9**
Typical plagiocephaly, obvious in normal three-dimensional vision. Note the forward turned ear on the "down" side of the head.

![Figure 10](image-url)

**FIG. 10**
Figure 10—The oblong head of the premature child who has no turning reflexes. Figure 11—The gravity effect which may cause plagiocephaly and the out-turned lower ear. (By permission of Mr R. L. Hay.) (From James, J. I. P. (1967): *Scoliosis*. Edinburgh and London: E. & S. Livingstone Ltd.)

the position *in utero* and thus perhaps also the scoliosis. It has been the only obvious supporting evidence for the hypothesis involving the intra-uterine position.

Alternatively, it seemed that it might be due to moulding of the head in labour. Hay therefore took the opportunity of observing plagiocephaly in the newborn. Imagine our surprise when not one single newborn infant of the 400 seen so far showed plagiocephaly
when forty to fifty should have done. It now seems likely that the kind of skull asymmetry that usually accompanies infantile scoliosis does not exist at birth but comes on within a few days or weeks after birth. If this has demolished our long held belief that it occurred during labour it has also removed the only evidence adduced by Denis Browne to support the intra-uterine position as a cause of scoliosis.

Much more work has to be done to determine when plagiocephaly occurs, but there is now a strong suspicion why it occurs. A premature baby without turning reflexes gets an oblong head from lying on one side (Fig. 10). Hay thinks that plagiocephaly probably arises by the baby’s lying in an oblique position and the still plastic skull “flowing” into this shape (Fig. 11). The appearance is sometimes grotesque; yet by the age of five it has almost always disappeared. Plagiocephaly, perhaps a result of gravity acting on a soft skull, could point to the same gravity effect on the infant’s spine, although this is doubtful because it appears so often in the latter part of the first year of life when the spine must be firm and is convex to the upper side. It does not seem possible yet to relate this post-natal posture to the development of scoliosis in infants.

Twin studies are of great value because a wholly genetic disease is one in which identical twins share the same deformity, whereas dissimilar twins are as ordinary siblings to each other. Table II shows the few twin pairs with scoliosis reported. As in club foot it suggests both a genetic and environmental factor, but the figures are too small to signify much.

**TABLE II**

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<th>Twins with Idiopathic Scoliosis</th>
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<tr>
<td>Faber (1936)</td>
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<tr>
<td>Scoliosis in both twins</td>
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<tr>
<td>Scoliosis in one twin</td>
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<tr>
<td>Fisher and de George (1967)</td>
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<tr>
<td>Scoliosis in both twins</td>
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<tr>
<td>Scoliosis in one twin</td>
</tr>
<tr>
<td>Wynne-Davies (1968)</td>
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<tr>
<td>Scoliosis in both twins</td>
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<tr>
<td>Scoliosis in one twin</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Scoliosis in one twin</td>
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Our studies of congenital scoliosis are in a stage of completion and the findings are provisionally similar to those in spina bifida and myelomeningocele. The genetic element is minor, if present at all, and the etiology is almost certainly related to the intra-uterine environment. It is therefore quite different from idiopathic scoliosis.

Another need is a study of adolescent kyphosis because it is a deformity of vertebrae in the same age group as idiopathic scoliosis; indeed a double lateral curve is common in adolescent kyphosis. A study of etiological and hereditary factors to establish any similarity of causation would be valuable.

Much recent speculation has been concerned with the concept that the initial deformity is lordoscoliosis. It has some attraction in making a mechanical explanation easier. What has not been shown is that lordoscoliosis does exist. We have given much thought to methods of measuring antero-posterior deformity in the laterally deformed spine, but have so far found insuperable difficulties because the antero-posterior radiograph is almost a lateral view of the apical vertebrae in a severe curve.
The last two decades have seen a completion of clinical observations of the pattern and behaviour of this disease and we do now know a great deal. It is doubtful if we shall gain much further insight into etiology from such studies. The known diseases which cause scoliosis—and there are many—deserve a much more intensive clinical study; it is inconceivable that light would not be shed on the mechanics of curve development, though perhaps not on a primary cause. Experimental scoliosis in animals has contributed little and one cannot foresee that it will.

We are left then to investigate further a familial basis to scoliosis. Genetic alteration is by an abnormality of structural protein or enzyme synthesis mediated by a change in the four bases and the twenty amino-acids that control our genetic destiny. There is, one may hazard, an alteration of collagen, mucopolysaccharide or other soft-tissue constituent of the vertebral column which itself or with the trigger of some unsatisfactory element of the environment causes scoliosis. Many inherited diseases, such as fragilitas ossium and Dupuytren’s disease, involve structural protein. None is yet chemically identified, unlike the many inherited abnormal enzyme diseases. All inherited diseases are chemical abnormalities, and I join with Ponseti in thinking that a biochemical change, probably inherited, will one day be shown to be the cause. Associated mental deficiency reinforces this possibility, because it is known to be often biochemical in origin. We must be prepared not to find anything and to start all over again on this knotty problem.

The infantile scoliosis so common in Europe must be intensively investigated. If genetically determined, why is it so rarely seen in North America? Why does it so often resolve? Why does it differ in such curious details from the adolescent form?

The pattern of inheritance of scoliosis is such that, as in club foot, environment must play a role. This could be a significant lead in attempting to discover etiology.

To elucidate the etiology of scoliosis means a long, patient, systematic study of all factors. Only one thing is sure: we will be baffled and defeated as in the past many times before we are successful in our search to comprehend the cause.

REFERENCES


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