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INNOVATIONS

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A new concept for the etiopathogenesis of the thoracospinal deformity of idiopathic scoliosis: summary of an electronic focus group debate of the IBSE

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This paper provides an edited summary of the first electronic focus group (EFG) of the International Federated Body on Scoliosis Etiology (IBSE). In it, the extensive research of Professor Sevastik and his colleagues on the thoracospinal theory of right thoracic adolescent idiopathic scoliosis in girls was debated via e-mail by IBSE members during the period November 2000 to March 2001. The summary (Comments, Questions and Answers 1–14) was circulated by e-mail to IBSE members on 4 April 2001. Comment 15 was subsequently received on 3 June 2002. Ideas presented in this summary are personal opinion and are not necessarily shared by all those within IBSE

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Abstract There is no generally accepted scientific theory for the etiology of idiopathic scoliosis, and treatment is pragmatic and unrelated to such knowledge. As part of its mission to widen understanding of scoliosis etiology, the International Federated Body on Scoliosis Etiology (IBSE) introduced the electronic focus group (EFG) as a means of increasing debate of extant knowledge on important topics. This has been designated as an on-line Delphi discussion, and has proven very successful. The text for this EFG was written by Professor Sevastik and drawn from the extensive research carried out by himself and his co-workers. The thoracospinal concept of etiopathogenesis applies only to girls with right thoracic adolescent idiopathic scoliosis (Rcx-T-AIS-F). According to this concept, increased longitudinal growth of the left periapical ribs triggers the thoracic curve simultaneously in the three cardinal planes. The concept does not deal with factors involved in curve progression. Sevastik advocates mini-invasive operations on the ribs as a treatment for early progressive thoracic curves. Areas of controversy include whether or not there is overgrowth of the left periapical ribs in Rcx-T-AIS-F, and the question of whether there should be a clinical trial of mini-invasive operations on the ribs.

Keywords Scoliosis · Idiopathic · Etiology · Ribs · Adolscence · Breast · Asymmetry · Surgery

Introduction

In the absence of any generally accepted scientific theory for the etiology of idiopathic scoliosis, treatment remains pragmatic and unrelated to such knowledge. The International Federated Body on Scoliosis Etiology (IBSE, see Appendix) introduced the electronic focus group (EFG) as a means of increasing debate of extant knowledge on important topics. The text for debate was written by Professor Sevastik, and was drawn from the extensive research carried out by himself and his co-workers. It was sent out by e-mail to all IBSE members, together with an invitation to send questions by e-mail to Dr. Dangerfield who, as the EFG moderator, collated them and sent them to Professor Sevastik for his response. The original paper was then sent again to all IBSE members, together with the questions and answers generated by the first round of

the debate. No further submissions were received. The paper represents the editing by Professor Burwell and Dr. Dangerfield of the comments and questions raised by the original Sevastik text of the EFG and of the answers by Professor Sevastik. Each comment is followed by the respective question(s) and then the answer(s) provided by Sevastik. Comment 15 is an additional comment submitted following the circulation of the debate to the members of IBSE.

The thoracospinal concept of etiopathogenesis applies only to girls with right thoracic adolescent idiopathic scoliosis (Rcx-T-AIS-F). According to this concept, a sympathetic nervous system disorder causes increased vascularity of the left anterior hemithorax in adolescent girls and results in increased longitudinal growth of the left periapical ribs. This leads to disturbed equilibrium of the forces determining the normal alignment of the thoracic spine and triggers the thoracic curve simultaneously in the three cardinal planes. The concept does not deal with factors involved in curve progression. Sevastik advocates mini-invasive operations on the ribs as a treatment for early progressive thoracic curves. Controversy remains over several issues, including:

1. Whether the increased vascularity of the left anterior hemithorax is primary or secondary to the thoracic curve in Rcx-T-AIS-F
2. Whether there is relative overgrowth of the left periapical ribs; and
3. Whether there should be a clinical trial of mini-invasive operations on the ribs

The relevance of animal experiments and finite element models to the concept are discussed.

Comment 1

Sevastik proposes that "*Sympathetic dysfunction, of as yet unidentified origin, results in hyperemia of the left hemithorax, which in turn is followed by increased growth of the ipsilateral ribs, thus constituting the triggering mechanism of the development of the complex deformity of the thorax and the spine in Rcx-T-AIS-F*".

Question

Sevastik states there is no evidence that other forms of AIS than RT/AIS in adolescent girls share the same etiology and pathogenesis. Has he made any attempts to evaluate other types of AIS?

Answer

No! No attempt has been made to evaluate issues related to the etiology and pathogenesis of other forms of scoliosis, either idiopathic or of known etiology. The aim of our studies has been to evaluate somatic variables related to Rcx-T-IS in adolescent girls and not to compare these with other forms of IS.

This does not challenge the statement that, at present, there is no evidence that all forms of IS share the same etiopathogenesis. Further research on this topic may or may not support this view.

Comment 2

Asher [2] requires that any theory about the etiology(ies) of idiopathic scoliosis has to explain:

(a) The emerging dependence of the deformity upon growth and growth rate
(b) Its predilection for females
(c) Members of involved families
(d) Its variable progression

Questions

Sevastik's thoracospinal theory explains (b). Could he please address (a), (c) and (d)?

Answers

(a) Reported studies on height, weight, limb asymmetries and other somatomatic parameters are diverging, and often contradictory. Burwell and associates state: "*There is clearly a need for further studies of skeletal right-left asymmetries and other anthropometric components as phenodeviants in deciphering the pathomechanisms of AIS in all its forms*" [5]. Growth is determined by the interplay of numerous physiological processes, i.e. impulses from the central, peripheral and autonomic nervous system, hormonal and humoral influences, vascular supply, cell proliferation and differentiation, all determined by genetic rules. The dependence of the scoliosis deformity upon growth is evident, since the condition affects *growing* humans. However, the role played by dysfunction of any of the mentioned processes, either separately or in combination, in the causation of the abnormal growth of thoracic and spinal structures in IS is unknown.
(c) It is known (Miller 2000 [15]) that IS aggregates within families, although the pattern of inheritance is unclear, and that this disorder is complex in nature with a significant degree of heterogeneity. Miller's authority in the field of genetics does not allow comment from the author.
(d) The variability of progression of IS curves is not easy to explain. However, for the sake of speculation, it seems reasonable to assume that the development of

an initial curvature depends on the relation between the magnitude of loads acting on the spine and the resources of each individual patient (age, skeletal maturity, height/weight index, physical fitness, sports, etc) to counteract or not the disturbed alignment of the spine. Biomechanical and epidemiological studies may throw some light on this important issue (see Question 12).

Comment 3

The case report of the 6-year-old girl with a right thoracolumbar (RTL) 46° curve that benefited from 2-cm shortening of three ribs on the concavity is a critically important finding.

Questions

(a) Could this have been a resolving curve?
(b) Have other children had this operation? If not why not?
(c) The infant and young child with progressive scoliosis curves still challenge the spinal surgeon. Could we address this surgical question in another electronic focus group?

Answers

(a) Yes! The Rcx-T curve of this 6-year-old girl might have resolved. However, it is not probable that a curve that progressed from 30° to 46° within 1 year would resolve later on.
(b) No! This is the only case. The reason is that Dr. Xiong as a neurosurgeon has only been able to perform this one operation. Personally, I do not operate any more, having retired in 1986. Over the last 5 years, I have tried to persuade scoliosis surgeons in the UK, Denmark, Norway, Greece, Belgium and Sweden to evaluate the effect of concave shortening and other rib operations in a series of patients with early progressive Rcx-T-IS curve. Although they showed an interest, none has yet proceeded to realize the project. Why? There may be a variety of reasons.
(c) Open discussion in another electronic focus group, or engagement of interested surgeons in evaluating the outcome of rib operations in a series of young patients with progressive Rcx-T-AIS-F under a standardized protocol, are both highly welcome suggestions.

Comment 4

In their article "The length and ash weight of the ribs of normal and scoliotic persons," Normelli et al. [17] state, "*In five of the six patients with right convex thoracic scoliosis, the left ribs of the three examined pairs were on average longer than the right ribs, but the difference was not significant*."

In contrast, Stokes et al. [35], in their abstract "Rib cage asymmetry in idiopathic scoliosis," said that "*11 of 19 patients with right single thoracic curves had rib arc lengths more than 3% greater on the right side at the curve apex*."

Question

Are the ribs on the concave side of the RT/AIS curve really longer than the ribs on the convex side? Is not more research needed to establish the findings?

Answer

In our study [17], the mean length of three periapical *concave* (left) ribs in five out of six persons with Rcx-T-AIS was greater than the corresponding value of *convex* (right) ribs; the difference was not significant in this small sample. However, the mean concave (left) *minus* convex (right) rib length in women with Rcx-T-IS was significantly greater than the corresponding left *minus* right length in non-scoliotic women [17, 29].

Stokes et al. [36] evaluated the concave and convex rib length using mathematical models rather than true measurements; longer convex ribs cannot explain the vertebral rotation to the convexity and, similarly, the rib hump on the same side.

If the evidence provided by these studies is not considered conclusive, further research on rib length asymmetry is recommended.

Comment 5

Sevastik suggests that RT/AIS in girls is a single disorder – that it has one single route of pathogenesis and set of pathomechanisms.

Question

Is that correct? If so, then the geneticists should concentrate on RT/AIS girls with progressive curves.

Taylor [38] points out that the major problem with any hypothesis about the etiology of AIS is that there are no specific biological markers for the condition and neither are there any for factors that lead to curve progression. This statement is consistent with the probability that the development of AIS involves the action of a combination of different mechanisms in different proportions in differ-

ent people to produce a final common deformity. This view is held by many workers (see Tredwell [39]).

Answer

The thoracospinal concept provides evidence that the triggering mechanism of the deformity, at least in Rcx-T-AIS-F, is asymmetrical growth of the ribs. Is not the hypervascularity of the left anterior hemithorax a biological marker?

The results of the clinical and the experimental studies support this concept and in an adequate way explain the pathogenesis of the deformity.

It is true that the development of AIS probably involves the combined action of different mechanisms in different proportions in different people to produce a final common deformity. However, this view is not yet supported by evidence.

Genetic studies focused on the most common IS, the Rcx-T-AIS, in an ethnically homogeneous population of girls may contribute to a better understanding of the complex hereditary transmission of the condition. In our pilot study of 218 females with AIS, the familial incidence of Rcx-T and -TL curves was found to be twice as high as that of left thoracic and double primary curves. Lack of a material large enough for a reliable design of the study did not allow statistical evaluation of these results; this study has not proceeded further (Diab and Sevastik 1998, unpublished). Extension of the study to a larger sample of patients may be of value.

Comment 6

Sevastik elsewhere separates the mechanisms of etiology, pathogenesis and pathomechanisms of IS – a concept that helps focus on the complexity of the genetic, environmental and tissue origins of IS. (It would help if he would place these definitions on the Internet.)

Sevastik's thoracospinal theory addresses pathogenesis and pathomechanisms.

Questions

(a) What determines curve progression in his theory?
(b) Has he any views on etiology?

Answers

The processes involved in the causation and development of the thoracospinal deformity in IS are specified by three well-defined pathophysiological terms:

- *Etiology*, i.e. the factor(s) causing the deformity
- *Pathogenesis*, i.e. the mode of origin of the process triggering the deformity, and
- *Pathomechanism(s)*, i.e. the sequence of events in the evolution of the structural changes resulting from the pathological process [28, 31]
  (a) The theory does not deal with the factors involved in the progression of the curve, i.e. the pathomechanism(s) of the deformity, which are probably of biomechanical nature (see also Questions 2d and 12).
  (b) The results of the studies on the pathogenesis of Rcx-T-AIS in girls suggest that the etiology of this deformity is linked to neural dysfunction associated with a sympathetic disorder.

Comment 7

The morphological work on radiographs carried out by Xiong and co-workers [46, 47] suggests that the three-dimensional (3D) structural changes of the vertebrae in early AIS develop simultaneously.

Questions

(a) Surely this cannot be used as an argument solely for a rib-growth driven curve initiation?
(b) Would it not also occur if:
  (i) The curve progression were spine-growth driven? or
  (ii) Both rib and spine deformation together were neuromuscular-driven?

Answers

The conclusions drawn from the results of Xiong´s morphometric radiographic studies are supported by the results of two other experimental studies [26, 27].

(a) Rib growth asymmetry is the only mechanism proven to cause simultaneous 3D vertebral rotation.
(b)(i) Disturbed vertebral growth in either the coronal, sagittal or horizontal plane should result in initial deviation of the spine in one plane, while deviation in the two other planes would develop as a secondary effect.
(b)(ii) Yes! In an experimental study in rabbits, electrical stimulation of paravertebral and intercostal muscles resulted in simultaneous 3D deformity of the spine [44]. Moreover, the results of some clinical studies suggest that the etiology of IS may be associated with a generalised muscular disorder [11, 24, 48]. However, these studies do not provide evidence as to whether the origin of the deformity is either neural or muscular. In this context it has to be pointed out that the use of the term "neuromuscular" is rather unspecified.

Comment 8

Tredwell [39] points out: "*The ability to produce a curved spine in the laboratory by means of rib resection, neurectomy, central nervous system insult, or electrical stimulation, says nothing other than identifying yet another insult to the spine that will cause it to curve*."

Sevastik makes this point clearly. Progress in studying the causation of AIS with a therapeutic end in view can be made, if not exclusively, by studying humans, but such studies are of course restricted by ethical restraints. Animal experiments may answer specific questions.

Sevastik analyzes the results of a series of clinical and experimental studies which "*provides unambiguous evidence for the thoracospinal theory of the etiopathogenesis of at least the most common form of IS, the right convex thoracic idiopathic scoliosis in adolescent females*."

The animal experimental work that Sevastik and his colleagues have published certainly shows that ribs can be manipulated to induce (trigger) and correct a scoliosis deformity. However, as Sevastik [30] writes, "*...any extrapolation of the results from experimentally induced scoliosis in animals to the etiology, the pathogenesis and the pathomechanisms of IS in man has to be advanced carefully. Such a relationship can only be justified if supported by relevant clinical verification*."

The experimental work on humans that Sevastik [29] reviews relates to breast size [18], breast vascularization [19], rib lengths [17], and negative findings using radioisotopic scanning of vertebrae and costochondral junctions [16] in females with RT/AIS.

Questions

Could these breast and rib changes be secondary to the thoracic spinal deformity, and particularly:

(a) Was the larger left breast due to the underlying chest wall asymmetry? Or, was it real?
(b) Was the breast asymmetry directional or random?
(c) To test his thoracospinal concept critically by thermographic studies, should not the controls for the RT/AIS girls be adolescent girls with some type of secondary scoliosis (e.g. neurological), and not the healthy control girls who were used?
(d) Do boys with RT/AIS show the thermographic changes in the left breast?
(e) What of girls and boys with LT/AIS?
(f) Could the rib length asymmetry in the RT/AIS females be adaptive and therefore secondary?
(g) How does Sevastik account for lumbar AIS curves?

Answers

I quite agree with Tredwell´s statement on the value of experimental studies to explain clinical phenomena, which I have also argued earlier, though with the important addition that, "*A relation between experimentally induced scoliosis and IS can be justified if it is sufficiently supported by relevant clinical observations or vice versa*" [28]. Accordingly, the strength of the thoracospinal concept is that the conclusions are based on the results of alternate clinical and experimental studies, which support each other.

(a) The study of the size of the breasts was qualitative and not quantitative. Therefore, the factor of thoracic cage asymmetry cannot be excluded, but it cannot be evaluated with any degree of certainty.
(b) It was the left breast that was significantly more often larger than the right one in the scoliotic, but not in the normal, probands.
(c) I do not agree! Asymmetric thermal emission of the skin in neuromuscular scoliosis, if found, could be related to asymmetric muscular contracture, and hence blur the evaluation of the results of the current study.
(d) Only girls with Rcx-T-AIS were included in the current studies; the aim was not to compare this with other forms of IS.
(e) *See (d)*
(f) Yes! This possibility was taken into account at the beginning of the studies. Therefore, experimental regional sympathectomy was undertaken in rabbits to find out whether the conclusions drawn from the clinical studies could find support; and they did.
(g) This question raises other questions needing answers:
- Do lumbar curves in girls constitute a separate form of IS with different etiology and pathogenesis than Rcx-T-AIS?
- Does a lumbar curve represent the primary curve of the scoliotic spine deformity, or
- Regardless of its magnitude, is the lumbar curve a secondary adjustment to the initially disturbed equilibrium of forces from the thoracic curve?

At present these and other questions find no evidence-based answer. Biomechanical studies currently being carried out in collaboration with Dr. Aubin may clear up some of these questions (see Question 12).

Comment 9

In connection with breast vascularization, especially in the upper limbs, injuries and other disorders are sometimes associated with sympathetic effects to the vasculature of the affected limb, which are secondary [33].

Question

Could not the greater vascularity of the left breast result from altered sympathetic activity arising from afferents in the deforming spine causing desensitization of neurons in the central nervous system? This would be analogous to

the warm type of reflex sympathetic dystrophy [40]. It might also account for the increased breast size.

Answer

The proposed hypothesis, in my view, provides an attractive concept of a possible relation between dysfunction of the sympathetic system and the pathogenesis of IS. However, do not the results of the studies in rabbits [1] show that it is the induced sympathetic dysfunction that leads to the development of the thoracospinal deformity with the characteristics of human IS, and not vice versa?

Moreover, if the altered vascularization of the hemithorax on the concave side of the curvature was secondary to the spinal deviation, should not the lateral deviation of the spine and the vertebral rotation affect the sympathetic chain on the side of the convexity rather than on the concavity?

Comment 10

In recent years, several workers have focused their attention on different neural mechanisms that may be involved in the development of IS. These are reviewed by Robin [23], Edgar [6], Taylor [38], Williamson [45] and Lowe et al. [13].

Taylor [38] writes, "*The growing vertebral column is extraordinarily sensitive and responsive to the most subtle alterations in neuromuscular control*." Every orthopedic surgeon with pediatric experience is well aware of how growing bones and joints deform in the presence of muscle imbalance.

Questions

(a) Rather than dismiss neural mechanisms as "not substantiated by any convincing clinical or experimental evidence," as Sevastik does, should we not ask the EFG moderator to seek an author/authors to summarize what is known about neural mechanisms in the development of scoliosis? – not only idiopathic but also scoliosis secondary to diagnosed neurological disease?
(b) Sevastik's thoracospinal theory of causation is another neural concept for RT/AIS is it not?

Answers

(a) That influences arising from the nervous system (central, peripheral and autonomic) control somatic functions in health and disease cannot be denied. It cannot be denied either that such factors are also involved in disturbed skeletal growth, leading to the causation and development of the thoracospinal deformity in IS. The problem is that (i) numerous proposed hypotheses do not provide an evidence-based explanation of the way in which such factors cause the deformity, and (ii) an explanation is required of how the supposed causative factor is linked to the pathogenesis of the deformity of IS. In a recent review report, Lowe et al. [13] conclude that: "*The consensus is that etiology is multifactorial. With time, continued research will lead to the identification of the various factors involved in the causation of this disorder, which affects so many children and adolescents*." An EFG to handle these issues would, of course, be welcome, although no new findings can be expected besides those included in the reviews of the last year.
(b) The thoracospinal concept certainly touches the etiology of the Rcx-T-AIS in girls on the evidence-based involvement of the sympathetic system in the pathogenesis of the deformity. Moreover, this concept provides a link between etiology and pathogenesis of this disorder, but the mode of this linkage is unknown.

Comment & Question 11

Would Sevastik please comment on:

(a) Roaf [21], who summarized evidence that intercostal muscles may have a postural as well as respiratory function and considered their possible role in scoliosis evolution.
(b) Pal [20], who supported the view that "*...vertical stability of the thoracic spine is maintained by equal support through the ribs from both sides due to the equal load brought to the laminae by the ribs through the costotransverse articulations and ligaments. Any interference in this balancing mechanism disturbs spinal stability, which will bend towards the more heavily loaded side*."
(c) Gardner [7], who developed the view that the sternum has an important function in maintaining spinal posture, which it does through the upper six ribs which firmly brace the upper six thoracic vertebrae, permitting very little flexion, extension or rotation. Gardner relates this function of the sternum to surgery for scoliosis, kyphosis and spinal fractures.

Answers

(a) The work of Roaf [21] and the experiments he performed on himself [22] prompted our study to evaluate the effect of electrical stimulation of the intercostal muscles in the rabbit (see above: Question 7). Our results support Roaf's statement on the importance of these muscles in scoliosis. Moreover, we have derived a method for morphometric study of in

tercostal muscles for evaluating the functional condition – for example to appraise the effect of physiotherapy on these muscles.
(b) Six years after the publication of the results of rib length asymmetry in scoliosis [17], Pal [20], on biomechanical considerations, concluded that the stability of the spine is secured through the symmetrical support provided by the ribs through the costotransverse joints. However, the results of experimental studies on rib length asymmetry have shown that forces transmitted to the spine through the costotransverse joints result in erroneous direction of vertebral rotation [32]. If applied close to the costotransverse joint, the forces are transmitted through the costovertebral joint and result in a 3D deformity similar to that in humans [26].
(c) Gardner´s [7] review provides new aspects regarding the role of the sternum in the stability of both the thoracic cage and spine, with implications for future research (see below, Question 12).

Comment & Question 12

What research has been done using finite element models to test the thoracospinal concept of the etiology of RT/AIS?

Answer

In the last 4 years, Aubin et al. presented advanced biomechanical finite element models which allow for:

(a) Introduction of biological parameters in kinetic studies of the spine under simulated dynamic (muscular) effects [3, 4],
(b) Growth and its modulation by perturbed loads on the spine [41, 42, 43].

Subsequently, using the existing finite element model, studies were undertaken to evaluate:

(c) The alterations of the forces acting on the equilibrium of the spine by rib shortening [8], and
(d) The correction mechanisms generated by spine instrumentation or rib shortening for the treatment of IS [9].

A new study, in progress, aims to evaluate the correcting effects of rib shortening on the spine by introducing growth factors into the model. The finite element model developed by Dr. Aubin and his colleagues provides new possibilities to simulate and evaluate the biomechanics of the thoracic cage and the spine in IS under dynamic conditions – thus giving a biological dimension to the study of the kinematics of the spine under normal and pathological conditions. A series of new projects have been discussed with Dr. Aubin, including:

(a) The effect of vertebral and costal growth (and asymmetry) in the development and correction of scoliotic curves,
(b) The relation of the lumbar with the thoracic curve (primary/secondary),
(c) The role of ribcage, costal cartilages, and sternum in the flexibility and the rigidity of the thoracic spine, and
(d) Other issues related to the pathogenesis and development of the thoracospinal deformity in IS.

Comment 13

Although it is a long way off at present, we can't reach the primary etiologic factor of a somewhat hereditary disease such as AIS without verification of a gene anomaly, or anomalies.

Questions

How can Sevastik demonstrate an etiologic factor as a primary one? Isn't it mandatory to show:

(a) Some evidence of gene anomaly in humans with AIS?
(b) The defective-gene model in an animal that expresses the same disease?

Answers

(a) From recent reviews it can be concluded that the relation between genetic factors and etiology of AIS has not yet been deciphered [13, 15].
(b) There are some early reports of hereditary kyphoscoliosis in (i) fowl [12, 37], (ii) mice [14], (iii) rabbits [25], and (iv) some other hereditary malformations in animals.

The implications of these early reports for modern genetic studies in IS cannot be commented on by the author.

Comment 14

The thoracospinal theory is attractive if it leads to minimally invasive treatment. The problem is that, genetically, different curve patterns are inherited through a single kindred. But Sevastik's theory only applies to a right thoracic curve pattern. It doesn't work well for any of the other patterns.

Question

Is there a place in the theory for this problem?

Answer

Since there is no evidence that all forms of IS may not have a common etiopathogenesis, our studies have focused on Rcx-T-AIS in girls, representing the most common form of all ISs.

As for the genetic transmission of IS in general, and this form of IS in particular, no conclusions can be drawn for the time being.

Comment 15

This comment was received after the above summary of the electronic focus group debate was circulated among the members of IBSE.

I [Dr. IAF Stokes] would like to offer some commentary to explain why I doubt the hypothesis of ribcage asymmetric development as a cause of idiopathic scoliosis, as proposed in this EFG.

Firstly, in reference to Comment 4, the point was raised that Stokes et al. [36] had reported evidence of rib length asymmetries, with the right ribs being 1.39% longer on average in cases of right convex scoliosis, in contrast to Sevastik's observations. Our findings also showed that there was a complementary finding (ribs 3.57% longer on the left on average) in patients with predominantly lumbar curves. Other groups (including an adult "control" group) had average values of rib length asymmetry lying between those extremes. Our finding was obtained by 3D stereoradiographic reconstructions of the rib cage of adolescent patients, in contrast to the direct measurements of older cadaveric specimens reported in Normelli et al. [17]. Perhaps a related finding is the upper limb length asymmetry first reported by Burwell and Dangerfield in 1977 (see Cole et al. [5]). They found arm lengths longer on the right with right thoracic and thoracolumbar curves, suggestive of a pattern of slight upper-quarter hypertrophy not present in patients with lumbar curves.

We had the opportunity to remeasure rib length asymmetry in 24 of our patients in a longitudinal study, with follow-up of between 5 months and 2.9 years, and an average of 2.51 observations per patient. The (unpublished) findings showed that in 17 of 24 patients, asymmetry of rib length lessened over time. This was in contrast to the positive correlation that we would expect to find between scoliosis magnitude and rib length asymmetry if the asymmetrical growth of ribs were "driving" the spinal lateral curvature.

The interpretation I can offer for these apparently disparate findings is that the ribcage and spinal development may be less precisely controlled in people with IS, with rib lengths "oscillating" more than normal. However, it may be that it is only in the spine where small asymmetries are liable to develop into a progressing deformity, for biomechanical reasons. This would argue against asymmetrical ribcage growth causing the spinal asymmetry, despite being associated with it.

This viewpoint is supported by the work of Kasai et al. [10], who measured the lengths of the 7th to 12th ribs in 28 patients (6 male, 22 female) with idiopathic scoliosis with a right convex single thoracic curve and aged between 6 and 25 years. The measurements were performed by the multi-projection volume reconstruction method of computed tomography. A significant difference between the left and right side length (laterality) was observed in the 11th and 12th ribs, with left ribs being approximately 20 mm longer than the right; and they concluded that since these are floating ribs, the scoliosis affected the laterality of the 11th and 12th ribs. There was no significant laterality in the 7th, 8th, 9th, and 10th ribs, and there was no significant laterality in any of the ribs in 15 healthy volunteers.

Secondly, in reference to Question 12, it was asked what research has been done using finite element models to test these ideas. In a finite element model [34], we simulated 20% rib growth that was principally at the anterior parts of the ribs (representing the costochondral cartilages). The simulated growth was asymmetrical, producing a right rib 11% longer than the left. Twenty percent overall growth was chosen to represent adolescent growth. Eleven percent of asymmetry was chosen because it was the upper limit of asymmetry seen in our clinical studies. These simulations produced a spinal curvature to the right (the side of rib "overgrowth") and also a vertebral rotation in the expected direction and of the expected relative magnitude. However, the magnitude of the spinal deviation was small – about 3° by a Cobb-analogous measurement.

Our findings certainly do not refute Sevastik's proposal. Nevertheless, our work provides evidence of an overall pattern of asymmetrical development of the thorax in IS, but not a pattern that provides a mechanism of etiopathogenesis dependent on rib asymmetrical growth. I personally did not pursue those studies of rib growth, since I am currently attempting to identify the mechanisms of progression of a small spinal curve to a large one – a process that is apparently not driven by asymmetrical growth of the ribs.

Question

Could Professor Sevastik please address this evidence?

Answer

Dr. Stokes, referring to his own observations of longer ribs on the convexity of thoracic curves and on the concavity of lumbar curves [35, 36], is challenging the patho-

genetic role of increased longitudinal growth of the left periapical ribs in girls with Rcx-T curves as proposed by Normelli et al. [17].

While Normelli's anatomical study [17] showed a statistically significant left minus right rib length difference between normal male and female subjects, in Stokes' radiographic study [36], patients of both sexes were used, and the average length of the 2nd to 11th ribs was estimated. In Normelli's study only the three periapical ribs were used. Moreover, while rib length in Normelli's work was based on tape measurements of fully ossified ribs from elderly women, in Stokes' research the ossified part of the ribs in younger individuals was evaluated by a stereoradiographic technique and mathematical methods. He also excluded thoracic and lumbar curves of less than 10° which may interfere with the definition of predominantly single curves of either pattern.

In summary, differences in the techniques and methods employed by both Stokes and Kasai et al. [10] to measure the rib lengths, as well as possible gender differences make these studies not comparable with that of Normelli. The conclusion drawn from Normelli´s findings is supported by the results of subsequent clinical and experimental studies, which explain the direction of both axial vertebral rotation in Rcx-T curves and the increased concave rib length in left lumbar curves, which Stokes' observations do not.

Appendix

International Federated Body on Scoliosis Etiology: mission, organization, membership, origins and mandate

Mission

The aim of the International Federated Body on Scoliosis Etiology (IBSE) is to widen the understanding of scoliosis etiology into other fields of science by bringing together experts in various fields of biological and engineering science. It provides a forum for a wider debate about scoliosis etiology and the presentation and encouragement of scoliosis research. The goal is the prevention of idiopathic scoliosis.

In the 9 years of its existence, the IBSE has promoted research on the etiology of idiopathic scoliosis in collaboration with other individuals and bodies. This has resulted in a conference (the Tenth Philip Zorab Scoliosis Symposium, Oxford, 30 March – 1 April 1998), a book (*Etiology of Adolescent Idiopathic Scoliosis, Current Trends and Relevance to New Treatment Approaches*, edited by RG Burwell, PH Dangerfield, TG Lowe, JY Margulies – *Spine: State of the Art Reviews* 2000;14), a CD-ROM bibliography of over 3500 references (available from Dr. Dangerfield), three electronic focus group debates (a summary of the first of which is published here), and the establishment of a website (www.liv.ac.uk/FacultyMedicine/ibse/). In addition, as a direct outgrowth of this collaboration, a Current Concepts Review was published in the American issue of the *Journal of Bone and Joint Surgery* (Lowe et al. 2000).

Organization

IBSE is not affiliated to any society and is an ad hoc body. It has two Trustees and eleven Co-ordinators. The Trustees are Mr. M.A. Edgar MChir FRCS and Mr. A.D.H. Gardner FRCS. The Co-ordinators are Professor R.G. Burwell MD FRCS, Dr. P.H. Dangerfield MD, Dr. K.M. Bagnall PhD, Dr. T.G. Lowe MD, Dr T.B. Grivas MD, Dr. N.H. Miller MD, Mr. V.J. Raso MASc, Professor J.A. Sevastik MD PhD, Dr. I.A.F. Stokes PhD, Professor T.K.F. Taylor D Phil FRCS and Professor D. Uyttendaele MD. The late Dr. S. Willner MD PhD was a Co-ordinator. Professor Burwell and Dr. Dangerfield facilitate the activities of IBSE. Currently there are 124 members in 26 countries. The initial members were contacted by mail in the first Postal Meeting of IBSE, dated 14 December 1994. The Tenth IBSE Meeting was e-mailed to IBSE members on September 26 2000 and comments invited. All contacts and exchange of views are by e-mail. Funding of IBSE was by the Scoliosis Research Society (1995–1997) and subsequently the British Scoliosis Research Foundation, for which we are grateful.

Membership

To date, the IBSE membership has been established mainly by invitation. The 11th Postal Meeting of IBSE contains the current list of members with qualifications, affiliations, postal addresses, telephone/fax numbers, e-mail addresses and research interests. Membership is open to all scoliosis surgeons and scientists as well as surgeons and scientists in other fields who are interested in the etiology of idiopathic scoliosis, who can join by sending their details electronically to Dr. Dangerfield (spine92@liverpool.ac.uk). There is no membership fee. New members will be informed by e-mail of the current activities of IBSE.

Origins and mandate

In 1993, in a paper that appeared in the British edition of the *Journal of Bone and Joint Surgery* (Orthopaedic Proceedings, vol 76 Supplement I, 12; 1994), presenting a concept for the etiology of idiopathic scoliosis, Burwell and Dangerfield called for a Task Force to hasten the possible finding of new treatments based on some knowledge of causation of idiopathic scoliosis. A letter was subse-

quently received by Professor Burwell from Dr. Dale E. Rowe MD, Chairman of the Prevalence Committee of the Scoliosis Research Society, requesting "thoughts...on the etiology and any ways in which the Scoliosis Research Society can further research in this matter." During the following year, the possibility of encouraging more etiologic research was discussed further at scientific meetings and among scoliosis surgeons and scientists. A formal proposal for the creation of an International Federated Body on Scoliosis Etiology (IBSE) was developed, put to and approved by each of the British Scoliosis Society Executive, the British Scoliosis Research Foundation (BSRF), the European Spinal Deformities Society Executive, the International Research Society of Spinal Deformities, through its first President Dr. Morey Moreland MD, and the Board of Directors of the Scoliosis Research Society (SRS). The then President of the SRS, Dr. Edgar G. Dawson MD, on behalf of the Board of Directors, gave approval for the initial funding for IBSE "with Drs. Dale Rowe, Thomas Haher and Richard Brown to serve as ad hoc committee to work with you on this project." Subsequently, during the Presidency of Marc Asher (1996–1997), the SRS established an ad hoc Etiology Committee (Chairman Dr. Thomas G. Lowe MD), four members of which are also Co-ordinators or a Trustee of IBSE (Dr. T.G. Lowe MD, Mr. M.A. Edgar M Chir FRCS, Dr. N.H. Miller MD, Mr. V.J. Raso MASc).

An earlier draft of this account of IBSE was written by R.G. Burwell and P.H. Dangerfield and sent by e-mail to all IBSE members for comment, and those comments have been incorporated in this text.

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