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THE PATHOGENESIS OF CONGENITAL VERTEBRAL MALFORMATIONS

A Study Based on Observations made in 11 Human Embryos and Fetuses

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The pathogenesis of congenital vertebral malformations was investigated histologically in 266 human embryos and fetuses. Malformations were found in 11 specimens, and were grouped according to a detailed classification. All the malformations were observed as abnormalities of the cartilaginous anlage of the vertebral body, and permitted some conclusions as to their pathogenesis. A hemivertebra or other defect of formation of the vertebral body is considered to be caused by abnormal differential growth of the loose-celled area. Defects of segmentation are due to complete chondrification of the dense-celled area or to an absence of the dense-celled area. The notochord does not seem to be responsible for malformations. Compensatory growth of other vertebral bodies resulting from a partial defect or a peculiar shape of the body is already present in this very early stage of development. Some specimens show a relationship between the abnormal distribution of the intersegmental arteries and the abnormality of the vertebral segments. Considering the importance of the intersegmental artery in the formation of the definitive vertebral body anlage, as mentioned in a previous paper, it may be concluded that congenital vertebral malformations are likely to occur during the stage of resegmentation and to be related to the abnormal distribution of the intersegmental arteries.

Key words: human embryology; spinal malformations

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The pathogenesis of congenital vertebral malformations is essential for a proper understanding of the lesions encountered in clinical practice. Several authors have commented on the pathogenesis (Feller & Sternberg 1930, Valentin & Putscher 1936, Junghanns 1937, Ehrenhaft 1943, Schmorl & Junghanns 1971, Epstein 1976, and Tsou 1977), but it must be noted that their hypotheses were mostly based on the radiological study of clinical cases or the investigation of older fetuses. Moreover, the interpretation of normal vertebral development on which these theories were based could not be substantiated by recent studies of human embryos (Tanaka & Uhthoff 1981).

Congenital malformations of vertebrae are usually divided into failure of formation and failure of segmentation. Feller & Sternberg (1930) believed that failure of formation, e.g. hemivertebra, was due to a lack of cartilaginous anlage of the vertebral body and that the notochord was responsible for the initiation of malformations. However, Junghanns (1937) proposed that failure of formation was due to a lack of ossification secondary to a lack of vascularization. In failure of segmentation, several theories have been proposed. Valentin & Putscher (1936) postulated that failure of segmentation was caused by destruction of the already differentiated intervertebral disc. On the other hand, Ehrenhaft (1943)

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mentioned that this condition might develop on the basis of complete chondrification of the dense mesenchymal zone. Overgaard (1945) thought that regressive changes at the end of the growth period might be responsible. Recently Tsou (1977) explained the mechanism of non-segmentation as osseous metaplasia of the annulus fibrosus. Thus the pathogenesis of both, failure of formation and failure of segmentation, is still controversial, and a well accepted theory has yet to be established.

In a previous paper, we showed that malformations are already present at the stage of chondrification. Thus we believe that these malformations most probably occur during the stage of resegmentation, and that they may be induced by abnormalities of the intersegmental arteries.

The purpose of this paper is to describe the malformations found in our series, to discuss their pathogenesis and to propose a more comprehensive classification of congenital vertebral malformations.

MATERIALS AND METHODS

Two hundred and sixty-six spontaneously aborted human embryos and fetuses were collected. The Crown-Rump (C-R) length ranged from 7 to 490 mm. The fertilization age, which was estimated according to C-R length (Patten 1968) and to morphological features of the body (Hamilton et al. 1972), varied from 5 weeks to full-term.

The specimens were immediately fixed in 10 per cent formalin. Embryos of up to 20 mm C-R length were embedded *in toto* in paraffin. In bigger specimens, the vertebral column was dissected, radiographed and, if necessary, decalcified with 12 per cent EDTA for 2 to 10 weeks. They were then embedded in paraffin.

The specimens were cut alternately in cross, sagittal and frontal planes, and were stained with Hematoxylin Phloxine Saffron, Toluidine Blue, Mann-Dominici, or Goldner's methods.

RESULTS

Malformations of one or more vertebral bodies were found in 11 specimens. One showed malformations in two independent regions. The fertilization age ranged from 5½ weeks to 16 weeks. Since out of the 266 specimens, 201 were less than 17 weeks old, the incidence of spinal malformation was 5.5 per cent. No malformation was found in fetuses older than 16 weeks. Malformations were classified into three major types: Type 1: failure of formation, Type 2: failure of segmentation and Type 3: mixed. Types 1 and 2 were subdivided into (a) defect and (b) error. "Defect of formation" implies absence of the vertebral body or part of it and "defect of segmentation", total or partial absence of the intervertebral disc. "Error" signifies some other malformation (Table 1).

Table 1. Classification of congenital vertebral malformation

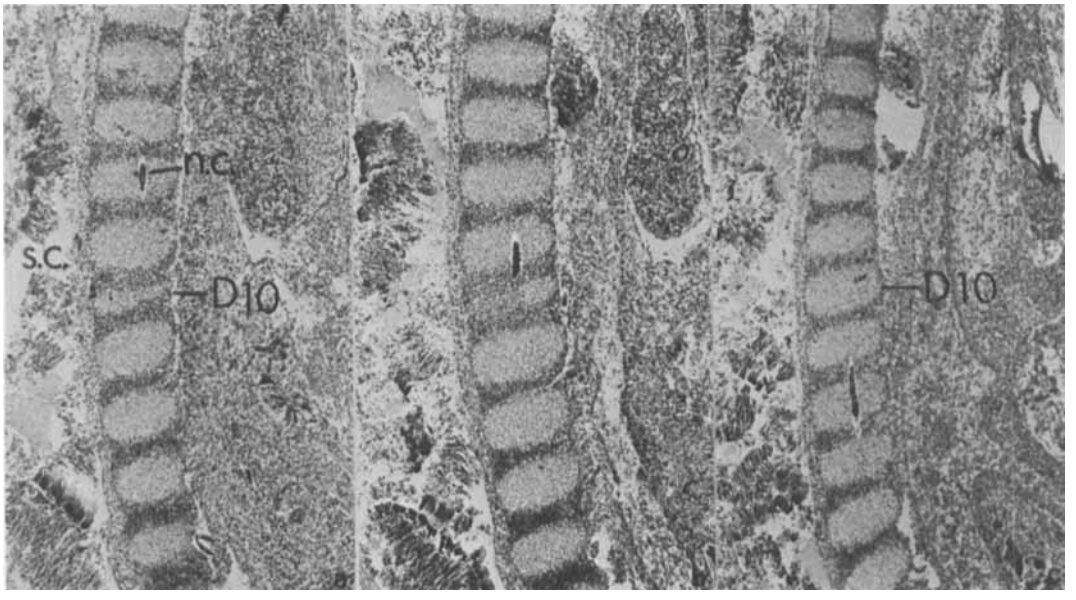
Type 1. Failure of Formation
a) Defect of formation
b) Error of formation
Type 2. Failure of Segmentation
a) Defect of segmentation
b) Error of segmentation
Type 3. Mixed

Type 1. Failure of formation

(a) Defect of formation

Specimen 1. C-R length 13 mm, age 6 weeks, sagittal section.

Some features of this embryo were reported in a previous paper as an example of failure of formation. The vertebral bodies consist of immature chondrocytes, and the intervertebral disc spaces are still occupied by undifferentiated mesenchymal cells. The body of D10 is markedly decreased in height on the left side. Chondrocytes which constitute the narrowed body are in the same developmental stage as those of other bodies (Figure 1a). Near the mid-portion, however, the posterior half of the body is virtually absent. It consists mostly of undifferentiated mesenchymal cells and partly of less differentiated chondrocytes. The anterior part shows a decrease in height (Figure 1b). On the right side, the body is formed almost normally (Figure 1c).



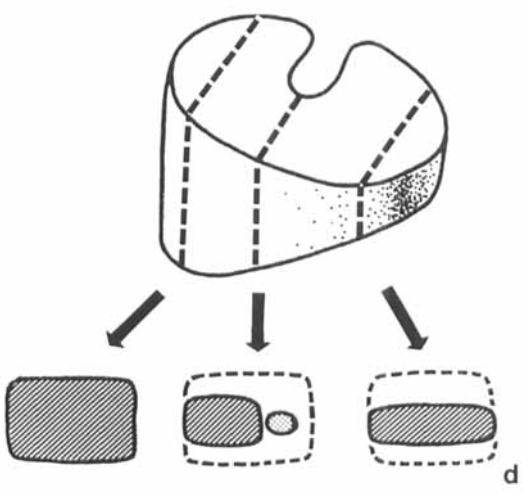


Figure 1. Type 1a (Defect of formation), 6-week-old embryo, sagittal section. A wedge vertebra is seen in the early stage of development. n.c.; notochord, s.c.; spinal cord. HPS × 27.
1a. Section cut on the left side. D10 shows a marked decrease in height.
1b. Section cut near the mid-portion. The posterior half of D10 is almost missing, and the anterior part is decreased in height.
1c. Section cut on the right side. The right part of the body is normally formed.
1d. Schematic drawings of this malformation.

These sections represent a wedge vertebra with a sagittal cleft of the posterior mid-portion as demonstrated schematically (Figure 1d).

Specimen 2. C-R length 15 mm, age 7 weeks, sagittal section.

This embryo shows a kyphotic deformity due to a failure of formation involving six thoracolumbar vertebrae. The kidney is seen anterior to the malformation. The middle four bodies show anterior defects and extrude dorsally. The adjacent two bodies also show incomplete formation. The spinal canal at this level is narrowed (Figure 2). Only one artery and a few veins can be recognized in the soft tissue anterior to these bodies.

(b) Error of formation

Specimen 3. C-R length 45 mm, age 9½ weeks, sagittal section.

In this specimen, L1 and L2 have peculiarly shaped vertebral bodies. On the left side, there are constrictions in the posterior aspects, and the

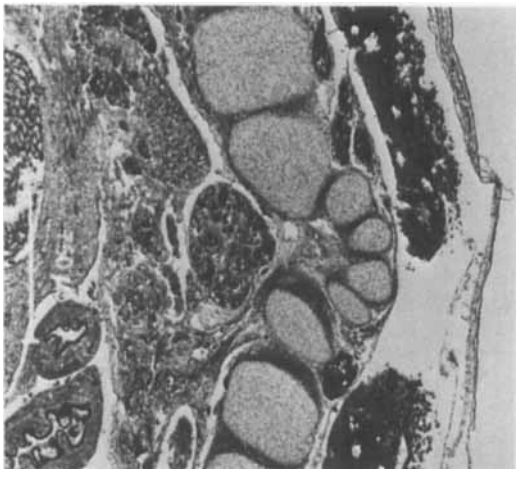


Figure 2. Type 1a (Defect of formation), 7-week-old embryo, sagittal section. Six defective bodies constitute a kyphotic deformity in the thoracolumbar area. The kidney is seen anterior to the malformation. HPS

posterior one-third of the bodies is changed in shape. The area of the constriction and the intervertebral disc spaces nearby are occupied by fibrocartilaginous tissue (Figure 3a). On the right side, these bodies are smaller in size, and the posterior part of L2 forms a cartilaginous mass which is separated from the body and protrudes into the spinal canal. Compression on the spinal cord is evident (Figure 3b). Vascular buds have penetrated the bodies anteriorly and posteriorly. Ossification has already started but seems to be somewhat retarded compared to other bodies. D12 and L3 also show slight changes in shape. The malformations are represented schematically in Figure 3c.

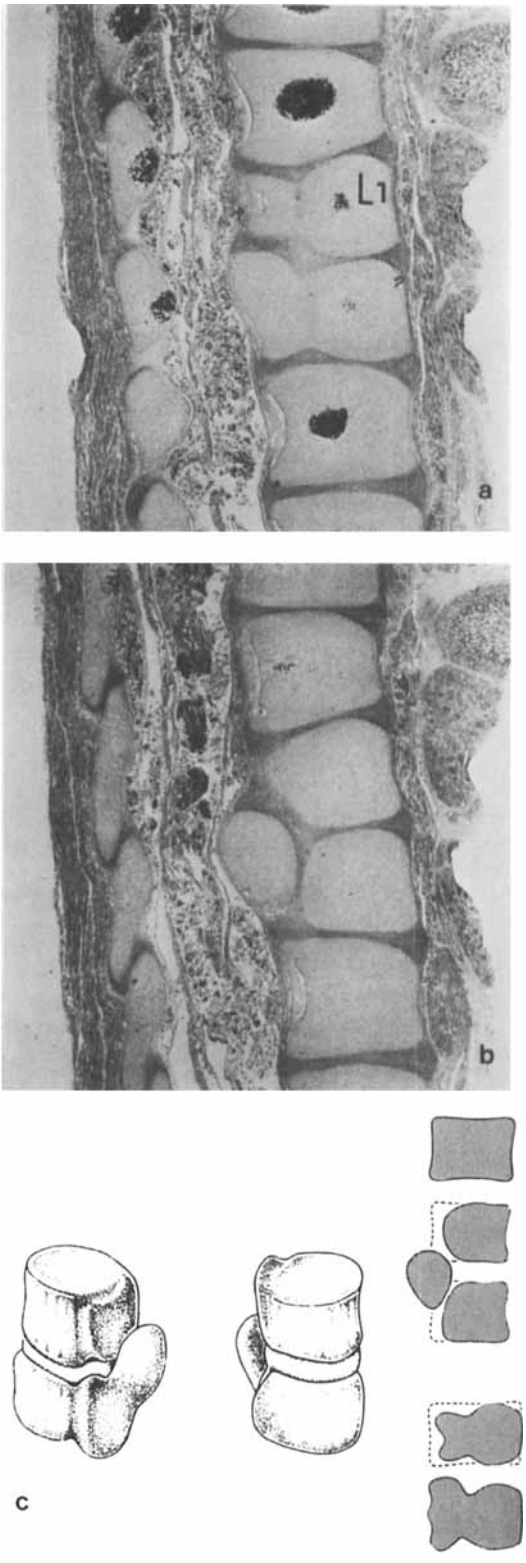


Figure 3. Type 1b (Error of formation), 9½-week-old fetus, sagittal section. Note the peculiar shape of L1 and L2. D12 and L3 also show slight changes in shape. HPS × 13.
3a. Section cut on the left side. Constrictions are seen in the posterior parts of L1 and L2.
3b. Section cut on the right side. The posterior part of L2 forms a cartilaginous mass which protrudes into the spinal canal.
3c. Schematic drawings of the malformation.

Type 2. Failure of segmentation

(a) Defect of segmentation

Specimen 4. C-R length 20 mm, age 7 weeks, frontal section.

A unilateral unsegmented bar extends over three segments on the right side in the high thoracic region. The bar occupies approximately one-third of the width of the body, and consists of chondrocytes which are in the same developmental stage as those of the segmented side. The intersegmental arteries are visible only on the left side and on the right side only venous channels can be recognized (Figure 4).

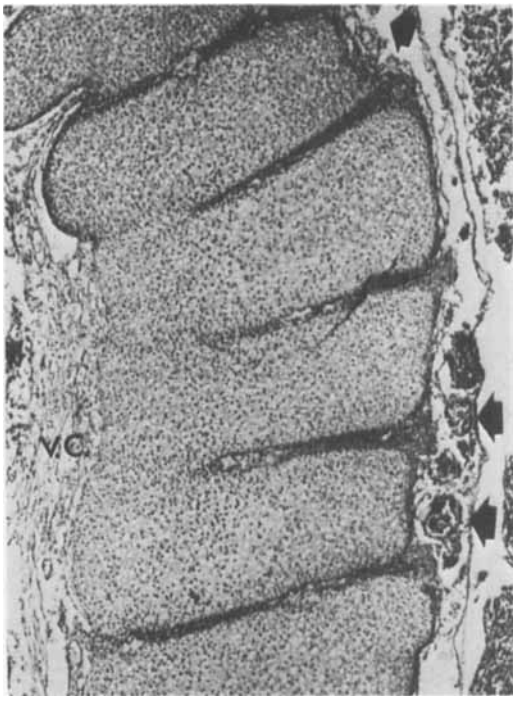


Figure 4. Type 2a (Defect of segmentation), 7-week-old embryo, frontal section. A unilateral unsegmented bar is seen in the high thoracic region. Note that there are only venous channels (v.c.) on the unsegmented side. Intersegmental arteries (arrows). HPS × 60.

Specimen 5. C-R length 140 mm, age 16 weeks, sagittal section.

A radiograph of this fetus shows a marked kyphoscoliotic deformity at the lower thoracic level. However, ossification centres of the vertebral bodies appear normal (Figure 5a). Histologically the cartilaginous bodies of D10, D11 and D12 show wedging in the sagittal plane. In sections near the mid-portion the inner one-third of the anterior half of the annulus fibrosus is composed of well-developed chondrocytes in D10–11 and D11–12. The outer two-thirds anteriorly shows less development of the annulus fibrosus than its posterior part (Figure 5a, b). This unsegmented bar is recognized in serial sections to be situated anterolaterally.

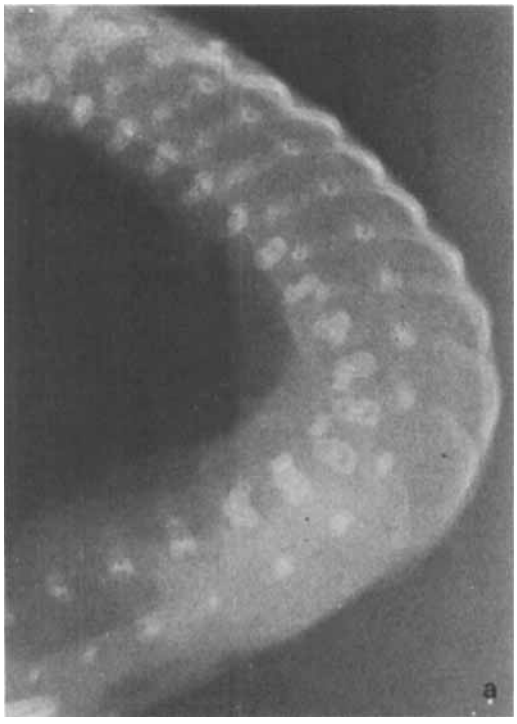
(b) Error of segmentation

Specimen 6. C-R length 70 mm, age 11½ weeks, frontal section.

This fetus shows malformations in two different regions: high thoracic and lumbosacral. The malformation of the thoracic vertebrae is described here, while the lumbosacral malformation will be described under Type 3 (Mixed Type).

The radiograph shows several abnormal findings. Ossification centres have appeared in the bodies of D2 through S2. Those of D3 and D4 are slightly smaller and are situated close to each other. D2 and D3 are not aligned with the axis of ossification centres of other vertebral bodies (Figure 6a).

The malformation is observed histologically to include four vertebral bodies. D3 and D4 show hemimetameric segmental displacement. The right half of D3 is obliquely fused with the left half of D4. The remaining left part of D3 is slightly smaller than the right half and fused with D2. The left rib of D3 is fused with that of D2. The right half of D4 is fused anteriorly with D3 (Figure 6b), separated in the mid-portion (Figure 6c), and posteriorly fused with D5 (Figure 6d). Two ossification centres, presumably those of D3 and D4, are seen in the obliquely fused segment. The notochord is situated between the two ossification centres, and takes a more anterior position in the region of D2 and D3. There is only one intersegmental artery on the left side, seen in the region of D2 and D3. On the right side, two arteries are seen over three segments of D3 to



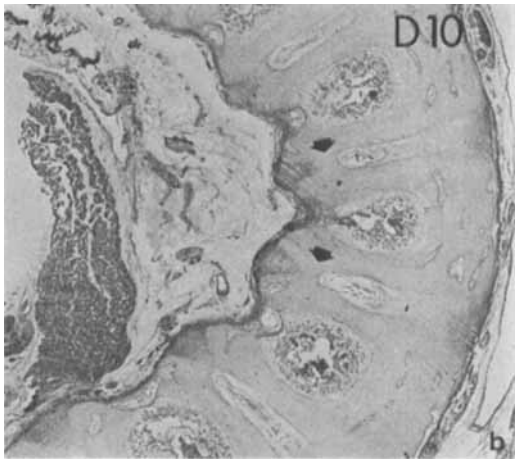
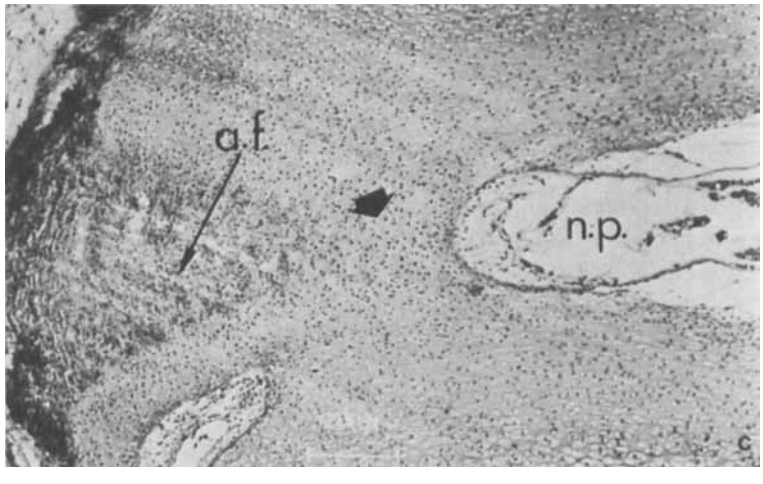


Figure 5. Type 2a (Defect of segmentation), 16-week-old fetus.
5a. A marked kyphoscoliotic deformity is recognized at the lower thoracic level. A radiograph, however, reveals normal ossification centres of the vertebral bodies.
5b. Mid-sagittal section. D10, D11 and D12 show the wedge shape of the body. The inner one-third of the anterior portion of the annulus fibrosus is replaced by chondrocytes in D10–11 and D11–12 (arrows). HPS × 9.

D5. In the section cut through the anterior portion, where the right half of D4 is fused with D3 (Figure 6b), one artery is situated in the middle of the fused bodies and the other one at the level of the cranial portion of D5. However, in the more posterior sections these arteries are more cranially located (Figure 6c). Finally one is situated just beside the body of D3, and the other just beside D4. There is no intersegmental artery at the level of D5 on the right side; however some vascular buds have started to penetrate the wall of the vertebral body (Figure 6d).



5c. Higher magnification. The anterior bar (arrow) consists of hyaline cartilage. The annulus fibrosus in the anterior portion is less developed than in the posterior portion. a.f.; annulus fibrosus, n.p.; nucleus pulposus.

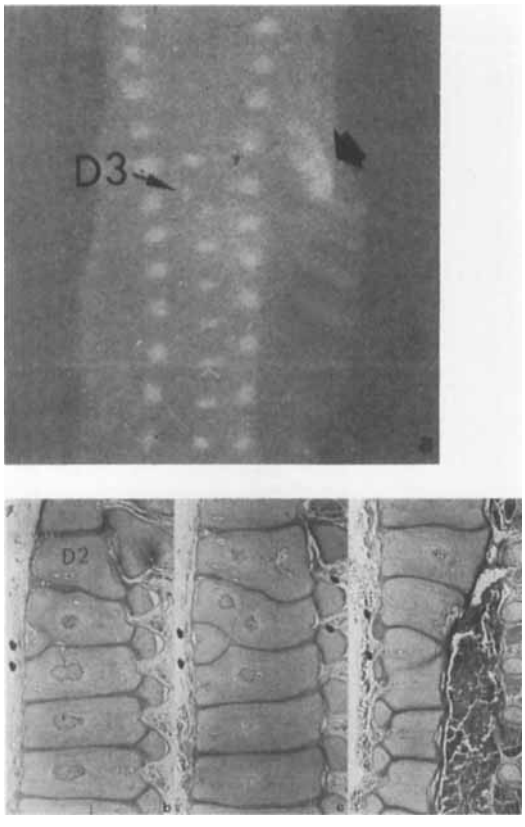


Figure 6. Type 2b (Error of segmentation), 11½-week-old fetus.
6a. Ossification centres of the vertebral bodies in D3 and D4 are slightly smaller than others. The axis of the ossification centres deviates at the level of D3–4. The second and third ribs are fused on the left side (arrow).
6b. Frontal section cut through the anterior portion (the specimen was cut obliquely because of rotation of the vertebral column). The segmental displacement is recognized in D3 and D4. The right half of D3 is fused with the left half of D4. The left half of D3 is fused with D2 and the right part of D4 with D3. Note the abnormal distribution of the intersegmental arteries (arrows): two arteries are situated over three segments on both sides (also see Figure 6c). Goldner × 12.
6c. Mid-frontal section. The right half of D4 is separated from D3 in this portion. Goldner × 12.
6d. Section cut through the posterior portion. The right half of D4 is fused with D5. There is no intersegmental artery on the right side of D5. Nevertheless, vascular buds have already started to penetrate the body. Goldner × 12.

Type 3. Mixed: Failure of formation and of segmentation

Specimen 7. C-R length 10 mm, age 5½ weeks, frontal section.

This embryo shows a hemivertebra (defect of formation) which is fused caudally with the adjacent vertebral body (defect of segmentation). The intervertebral disc spaces are still occupied by undifferentiated mesenchymal cells. On the right side, where half of the body is missing, the corresponding vessel and rib are absent as well. In other words, the number of these structures is less by one on the right side compared to the left side (Figure 7).

Specimen 8. C-R length 15 mm, age 6 weeks, frontal section.

Malformations are recognized in the sacrococcygeal region. In the section cut through the posterior portion, the left half of a body is missing (defect of formation). The two caudally-suc-

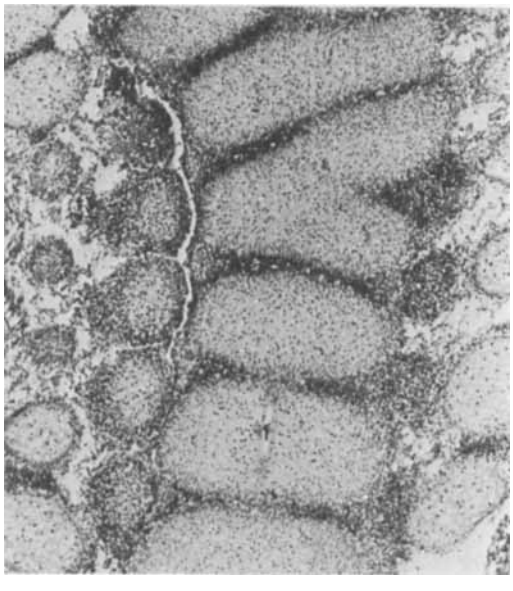


Figure 7. Type 3 (Mixed), 5½-week-old embryo, frontal section. The developmental stage of this embryo is very early so that the intervertebral disc spaces are still occupied by undifferentiated mesenchymal cells. A hemivertebra is fused caudally with the vertebral body. On the right side, the corresponding vessel and rib are missing as is half of the body. HPS × 60.

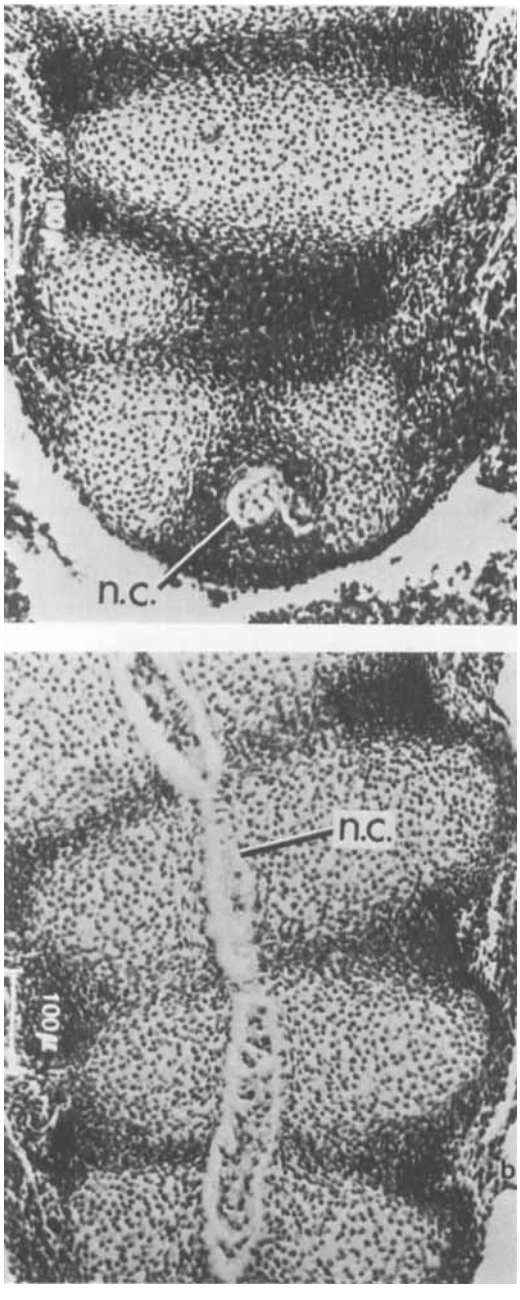


Figure 8. Type 3 (Mixed), 6-week-old embryo, frontal section. n.c.; notochord. Mann-Dominici
8a. Section cut through the posterior portion. A partial defect of the body and defect of segmentation are seen. The notochord is surrounded by undifferentiated mesenchymal cells.
8b. Section cut through the mid-portion showing features of these malformed bodies. The notochord does not seem to be responsible for the malformations.

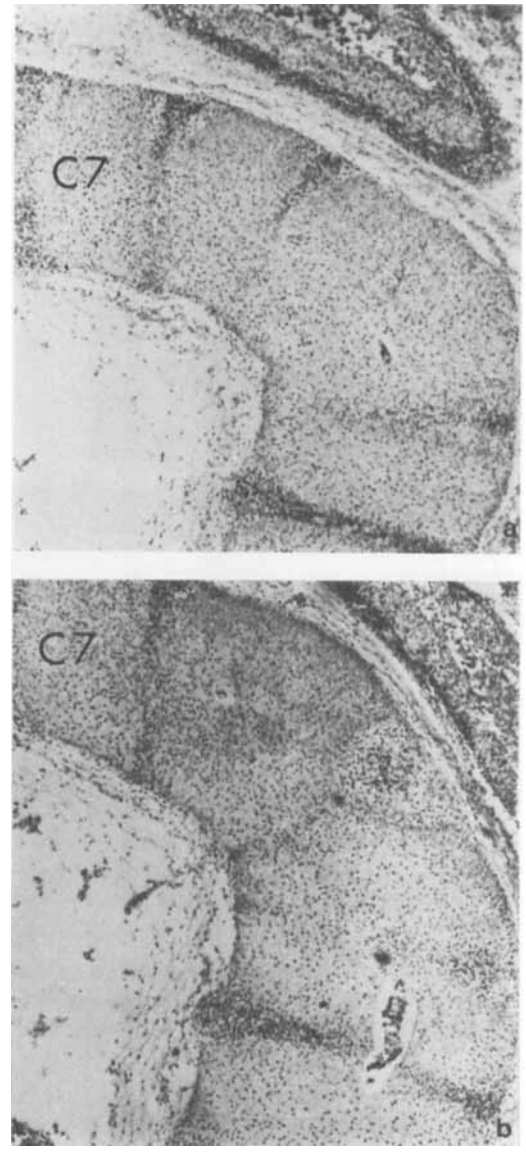


Figure 9. Type 3 (Mixed), 7-week-old embryo, sagittal section. Goldner × 60.
9a. A posterior unsegmented bar extends over D1 through D5. D2, D3 and D4 constitute a block vertebra.
9b. A section cut laterally shows a defect of D3 and a complete fusion of D1 and D2.

ceeding vertebral bodies are fused (defect of segmentation) and the central part is missing (defect of formation) where the notochord is seen surrounded by condensed mesenchymal cells (Figure 8a). In the section of the mid-portion, the

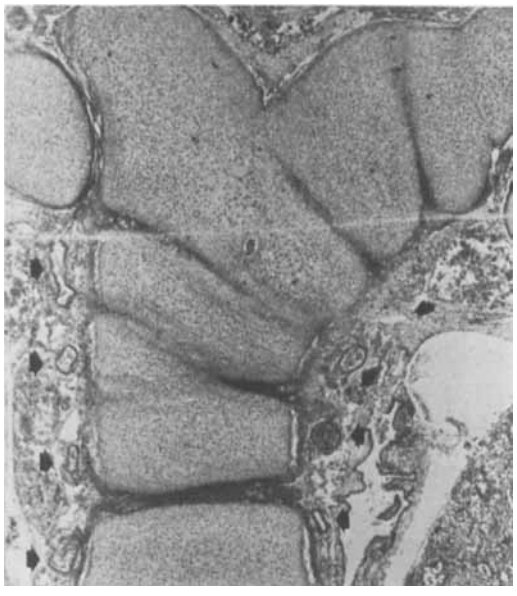


Figure 10. Type 3 (Mixed), 7½-week-old embryo, frontal section. The vertebral column shows a complex segmentation and a bifurcation at the high thoracic level. Note that the intersegmental arteries (arrows) are seen only opposite the vertebral segments. HPS

vertebral body with a defect of the left half in the posteriorly cut section appears to be normal except for fusion with the cranially situated body on the right side. The two bodies caudal to this vertebra show failure of segmentation on the left side, and half of the body is missing on the right side (Figure 8b). There is no evidence that the notochord is responsible for these malformations. There is asymmetry in the distribution of vessels.

Specimen 9. C-R length 19 mm, age 7 weeks, sagittal section.

This embryo shows a marked high thoracic lordosis. The malformation of D2, D3 and D4 is so complex that it is difficult to determine their exact shapes in sagittal sections. A posterior unsegmented bar is recognized between D1 and D5. The posterior part of D3 is missing, and the anterior half is fused with D2 and D4, representing a block vertebra (Figure 9a). In another section, D1 and D2 constitute a block vertebra and D3 is missing completely (Figure 9b).

Specimen 10. C-R length 25 mm, age 7½ weeks, frontal section.

This embryo shows anomalies of both formation and segmentation at the high thoracic level. The cervical vertebrae are not seen. The vertebral column shows complicated segmentation of the bodies (error of segmentation) and is bifurcated cranially (error of formation). Intersegmental arteries are seen only opposite the vertebral segments (Figure 10).

Specimen 11. C-R length 50 mm, age 10 weeks, sagittal section.

A partial defect of the vertebral body (defect of formation) and an anterior unsegmented bar (defect of segmentation) are recognized in this specimen. On the right side, approximately one-third of the posterior part of D4 is occupied by fibrocytes instead of chondrocytes. The shape of the body is trapezoidal, and the adjacent two bodies, D3 and D5, show the compensatory increase in height (Figure 11a). In the section of the mid-portion, the anterior halves of the intervertebral discs in D2–3 and D3–4 are replaced by cartilaginous tissue (Figure 11b). On the left side, the vertebral bodies have developed normally (Figure 11c).

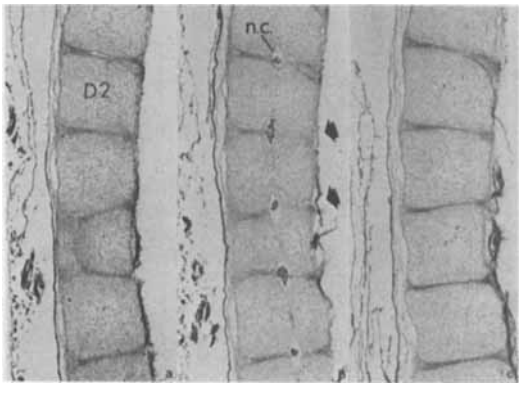
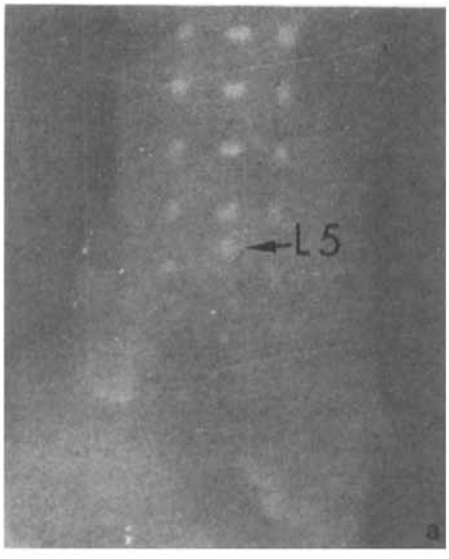


Figure 11. Type 3 (Mixed), 10-week-old fetus, sagittal section. Goldner × 27.
11a. Section cut on the right side. The posterior part of D4 is missing. Note that the two adjacent bodies show changes in shape.
11b. Section of the mid-portion. The anterior halves of the annulus fibrosus of D2–3 and D3–4 show a defect of segmentation (arrows). n.c.; notochord.
11c. Section cut on the left side. Here, the bodies are normally formed.



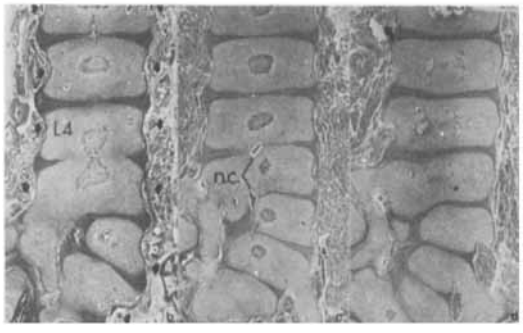


Figure 12. Type 3 (Mixed), 11½-week-old fetus.
12a. The ossification centre of L5 is closer to that of L4. S1 and S2 show an abnormal arrangement of ossification centres. Note the marked obliquity of the pelvis.
12b. Frontal section of the anterior portion. L4 and L5 are fused as well as their ossification centres. The intersegmental arteries (arrows) are recognized on the hemivertebral side, but not on the defective side. Goldner × 11.
12c. Section of the mid-portion. Note that the notochord is not always the boundary of a hemivertebra as seen in S2. n.c.; notochord. Goldner × 10.
12d. Section of the posterior part. Malformations in the sacral region are clearly seen. Goldner × 10.

Specimen 6. Lumbosacral vertebrae. Frontal section.

This fetus shows hemimetameric segmental displacement of the thoracic vertebrae described in Type II – (b). A radiograph shows a marked obliquity of the pelvis and an abnormal arrangement of ossification centres in the bodies of L4 through S2 (Figure 12a). Histologic sections show details of the malformation. L4 and L5 are fused in the anterior halves of the bodies (defect of segmentation), and ossification centres are partially connected as well (Figure 12b). S1, S2 and S3 are hemivertebrae (defect of formation), but an area of the defect of S1 is occupied by a cartilaginous mass which is continuous with L5. Instead of transverse processes on the right of S1, S2 and S3, there is a cartilaginous bar continuous with the transverse process of L5. It occupies the paravertebral region as far as the level of S4 to form the right sacroiliac joint (Figure 12c). On the left side, the transverse processes of S2 and S3 form the left sacroiliac joint (Figure 12d). S3 and S4 are almost completely fused (defect of segmentation). The axis of the sacrum is curved toward the right coxofemoral joint. The coccyx is absent in this fetus. The intersegmental arteries can be seen as far as S3 on the left side. However, no artery is recognized at the level of S1 and S2 on the right side (defective side). The intersegmental artery can not be defined below the level of S4 on both sides. At the level of L5, the notochord, which is situated in the midline cranially to L4, deviates increasingly toward the right side. It lies to the right of the hemivertebra at the level of S1. At the level of S2 and S3, the notochord is situated in the bodies of hemivertebrae (Figure 12c). Sections cut through the anterior and posterior portions do not show remnants of the notochord.

DISCUSSION

Junghanns (1937) published schematic drawings of the normal and abnormal process of the vertebral development. His interpretation was based on two concepts. Firstly, the vertebral body in the early cartilaginous stage consists of two lateral halves; between them the ventrodorsal extension of the perichordal sheath is situated. Secondly, two ossification centres appear, ventrally and dorsally, in the vertebral body. On this basis, he concluded that failure of formation was due to a lack of ossification secondary to a lack of vascularization. A ventral or dorsal hemivertebra,

could thus be explained. A lateral hemivertebra was thought to be due to failure of ossification on one side with failure of fusion of two chondrification centres. No evidence was supplied that the normal development of the vertebral body proceeds this way. As demonstrated in our previous paper, the vertebral body forms as one cartilaginous anlage. Moreover, defects of the body are already present at the stage of chondrification and, therefore, can not result from failure of ossification.

Van Schrick (1932) proposed two principal categories in the classification of congenital kyphosis: failure of formation and failure of segmentation. This concept is now accepted for all congenital vertebral malformations. However, subdivision is not uniform. We found that both failure of formation and failure of segmentation can be subdivided simply into (a) defect and (b) error (Table 1). Type 1, failure of formation, refers to abnormalities of the vertebral body, and is subdivided into (a) a partial or total defect (absence) of the body and (b) some other abnormalities of formation such as a specific change in shape. Type 2, failure of segmentation, signifies abnormalities of the intervertebral disc, and is also subdivided into (a) simple defect (absence) of the intervertebral disc either totally as in a block vertebra or partially as in a unilateral unsegmented bar, anterior bar, or posterior bar, and (b) some other error such as oblique direction of the disc in hemimetameric segmental displacement. Type 3, or mixed type, can be any combination of the above anomalies.

No malformation was found in specimens of the age over 17 weeks. The following reasons may account for this. Local laws require that spontaneously aborted fetuses over 500 g must be buried, so that it is more difficult to obtain older fetuses than younger ones. In fact, the age distribution of our collection is not even throughout the intrauterine period. Also a higher incidence of malformation can be anticipated in cases of an earlier spontaneous abortion.

Our study allows us to review the pathogenesis of congenital malformations of the vertebrae. First of all, a defect of the body, e.g. a hemivertebra, does not result from failure in ossification as postulated by Junghanns (1937). As seen in Figure 12, it is already present at the stage of calcification as a defect of the cartilaginous body. This must imply a failure of chondrification in the loose-celled area. The extent of the defect is illustrated in Specimen 1 which shows that the malformation is not limited to exactly half a body or a whole body. In fact different parts of the body can be involved to different degrees. Also the cell differentiation in the body varies. Therefore, the malformation must result from an abnormal differential growth of mesenchymal cells in the loose-celled area.

As for failure of segmentation, Tsou (1977) stated that non-segmentation was caused by a secondary bony change of the fibrous annulus, called osseous metaplasia of the annulus fibrosus. Failure of segmentation is, however, already present before cells in the intervertebral disc spaces begin to differentiate (Figures 7, 8). In normal development, mesenchymal cells in the dense-celled area begin to differentiate into fibroblastic cells of the annulus fibrosus shortly after chondrification of the vertebral body has been completed. Thus it can be considered that failure of segmentation is caused either by complete chondrification of the dense-celled area, or by an absence of the dense-celled area.

The influence of the notochordal tissue upon the vertebral development is still open to discussion. Schmorl & Junghanns (1971) argued that persistent notochordal tissue hinders vertebral development. Feller & Sternberg (1930) believed that the notochord is responsible for malformations of the vertebral body. They observed a mild curvature of the notochord toward hemivertebrae in an embryo of 21 mm length. Interestingly one of our specimens (specimen 8) resembles their embryo. However, we observed the opposite, a curvature toward the defective side (Figure 8b). Displacement of the notochord does not determine the direction of curvature nor the site of the defect of the body. Moreover, we found a specimen which exhibited a bifurcated notochord in the absence of any malformation. The intersegmental arteries are normally distributed (Figure 13). This seems to indicate that no relationship exists between malformation of the vertebral body and the notochord.

Defects of the body or changes in shape may

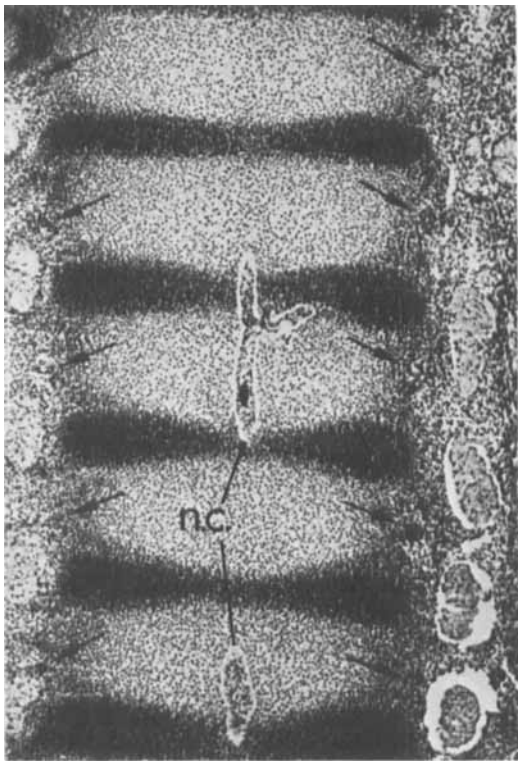


Figure 13. Seven-week-old embryo, frontal section. Note the abnormal notochord. The intersegmental arteries (arrows) are normally situated. n.c.; notochord. Goldner × *60.*

cause a compensatory growth of other vertebral bodies, particularly of the adjacent ones (Junghanns 1937). Such changes in shape of the body, however, can be recognized at a much earlier state of development (Figures 3, 11). Since ossification centres develop in an oval shape even in malformed bodies (Figure 5), the shape can not be precisely demonstrated radiologically until ossification of the body is complete. We feel that changes in shape occur at the time when malformations develop.

We agree with Junghanns (1937) on the importance of vascularization. We feel, however, that the distribution of the intersegmental arteries plays a decisive role during the stage of resegmentation and early chondrification, and not during the stage of ossification. Since the intersegmental artery is instrumental in the formation of the definitive vertebral body anlage during the stage of resegmentation (Tanaka & Uhthoff 1981) any abnormal distribution of the arteries may induce malformation.

There is a distinct possibility that malformations could arise from an abnormal migration of the sclerotomic cells. In the stage of migration, however, the sclerotomic cells do not show any difference in nature other than in density. Although the morphologic aspect of cells does not permit a conclusion as to their potential, we think that these cells have not yet been sufficiently differentiated to cause malformations.

According to these observations, we conclude that congenital vertebral malformations occur during the stage of resegmentation and are related to abnormalities of the intersegmental arteries.

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