Myelomeningocele before birth

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The authors report a study of 92 human embryos and four fetuses with myeloschisis. The characteristics of embryonic myeloschisis compared with spina bifida cystica in infants are: 1) the lesion is often more diffuse, involving the whole spinal cord (12 embryos); 2) the cervical cord is more frequently affected (23 of the remaining 80 embryos); 3) holoprosencephaly is frequently associated (18 embryos); 4) meningocele is not found; and 5) hydrocephalus and Arnold-Chiari malformation are not yet developed. Hydrocephalus and Arnold-Chiari malformation are found in myeloschistic fetuses. Almost all embryos with diffuse and cervical myeloschisis or with holoprosencephaly are extruded before birth by spontaneous abortion. Absence of meningocele in the embryonic period implies that its appearance is deferred to the fetal period. The development of hydrocephalus and Arnold-Chiari malformation also seems to be delayed until the fetal period. Our observation implies that myelomeningocele is induced by non-closure of the neural tube, not by rupture once it was closed. "Neural overgrowth" and disturbed "recanalization process" are discussed in relation to the pathogenesis of myelomeningocele.

KEY WORDS: myelomeningocele; meningocele; anencephaly; holoprosencephaly; hydrocephalus

MYELOMENINGOCELE after birth has been studied extensively and its features have been well documented. The state of myelomeningocele before birth is still poorly understood, because the opportunity to study such malformed embryos or fetuses is very limited. Only about 40 specimens (including anencephalic specimens) have been reported in the literature. Most reports contain one or two, or several at the most, embryos or fetuses with the malformation, while over 1000 infants with spina bifida cystica were collected and analyzed in one clinic. Since the basic feature of myelomeningocele is established in the early embryonic period and the embryo remains in the uterus for as long as 7 months, full understanding of the malformation will never be achieved without information on its development before birth. The present report is based on the review of more than 90 consecutive human embryos and fetuses with the anomaly, collected in Kyoto University, Japan. The collection is the largest in the world, and is large enough to make possible the overall survey of the malformation in the embryonic period.

Materials and Methods

The revision of the Japanese Eugenic Protection Law in 1952 allowed qualified gynecologists to terminate pregnancy for sociomedical reasons, requiring only the request of both the mother and her spouse. This resulted in a large number of recorded in-
TABLE 1

Methods by which embryos are obtained

<table>
<thead>
<tr>
<th>Methods by which embryos are obtained</th>
<th>Induced Abortion</th>
<th>Spontaneous Abortion</th>
<th>Ectopic Pregnancy</th>
<th>Hysterectomy</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>myeloschistic embryos (N = 92) (%)</td>
<td>77.8</td>
<td>19.6</td>
<td>1.1</td>
<td>0</td>
<td>1.1</td>
</tr>
<tr>
<td>average of our embryos* (%)</td>
<td>95.0</td>
<td>2.1</td>
<td>1.1</td>
<td>1.8</td>
<td>0</td>
</tr>
</tbody>
</table>

*Calculated from 20,102 embryos, abnormal embryos included.

duced abortions. These operations were usually done by dilatation and curettage, a procedure that severely damages embryos in most cases. However, in some instances, intact embryos were obtained by skilled gynecologists. This led to the establishment of a large team of selected gynecologists willing to donate their better specimens to the Human Embryo Center for Teratological Studies, Faculty of Medicine, Kyoto University. The collection was not limited to those obtained by operations for sociomedical reasons, but was extended to include spontaneously aborted embryos, and fetuses removed for various reasons.

The embryos were carefully washed with saline to remove maternal blood coagula, and fixed in Bouin's fluid at the clinic where they were removed. On the next day, they were transferred to a 10% formalin solution for storage. Careful examination was made under binocular stereomicroscope in order to determine whether the embryos were alive or dead in the uterus, the degree of trauma to the embryos during operation or by subsequent manipulations, what developmental stage the embryos belonged to, and whether any externally visible malformation was present.

Many of the embryos with various malformations were photographed, embedded in paraffin, serially sectioned at 10 µ, and stained, usually with hematoxylin and eosin. For the fetuses, the weight, crown-to-rump length, and externally visible malformations were recorded after fixation in Bouin's fluid or 10% formalin solution. The Center presently has over 35,000 embryos and 4000 fetuses. Among them, 92 embryos and four fetuses with myeloschisis (neural opening in the spinal cord) were found. In addition to these myeloschistic embryos and fetuses, there were also found many specimens with neural openings with lesions limited to the area rostral to the rhombencephalon, leaving the whole spinal cord intact. Such embryos and fetuses were not included in this study of myelomeningocele. Serial section for histological study was made on 55 of 92 myeloschistic embryos. For the remaining 47 embryos, the study was made only on macroscopic observation of the photographs or under the binocular stereomicroscope. For the four fetuses, the central nervous system was carefully dissected and observed under the operative microscope.

Observations

Summary of Material

Diagnosis of embryonic myeloschisis was usually grossly evident, with eversion and overgrowth of the neural plate, but in some instances, artifactual neural opening due to trauma had to be differentiated from genuine myeloschisis. Our differentiation was based on smooth contour of the everted neural plate and smooth junction between the everted neural plate and the neighboring tissue.

Table 1 shows how these embryos were obtained. Most of them were obtained by in-
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TABLE 3

Developmental stage of the myeloschistic embryos in the series

<table>
<thead>
<tr>
<th>Type of Myeloschisis</th>
<th>Carnegie Stage</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>11  12  13  14 15  16  17  18  19  20  21  22  23</td>
</tr>
<tr>
<td>diffuse localized cervical (combined type included)</td>
<td>2  1  2  4  1  1  1  2  23</td>
</tr>
<tr>
<td>caudal</td>
<td>1  3  8  2  8  13  6  2  9  1  2  4  57</td>
</tr>
<tr>
<td>total</td>
<td>2  3  3  11 4  14 14  7  2 13  6  4  2  7  92</td>
</tr>
</tbody>
</table>

duced abortion. There was history of genital bleeding in 29 embryos obtained by induced abortion, and in 15 of the 29, the operation was performed for "threatened abortion." Of the 92 myeloschistic embryos, 20% were recovered from spontaneous abortion. This rate of spontaneous abortion is about 10 times higher than its average rate (2.1%), calculated from 20,102 embryos in our collection including normal and abnormal embryos (Table 1).

Intrauterine death was established according to the criteria developed by Pearson, et al. Almost half of the myeloschistic embryos were dead in the uterus (Table 2). Some of them were already dead, although they were obtained by operation performed for socioeconomic reasons and there was no history of abnormal genital bleeding.

The trauma noted in the embryos was ranked in three degrees, in the order of increasing severity, as follows: Group A: Embryos recovered without any visible damage; Group B: Embryos with damage limited to the extremities and the trunk preserved intact; Group C: Embryos with injury to the trunks and possibly also to the extremities. Most of these myeloschistic embryos were recovered without much traumatized damage and could be categorized into Group A or B (Table 2).

Determination of developmental stages of the embryos (Table 3) was based upon the Carnegie criteria, which are currently the most reliable for assessment of embryos. The criteria are based mainly on rapidly changing external appearance of the embryos and consist of 23 identifiable stages of development ranging from the zygote (Stage 1) to the embryo about 55 days old with a 30-mm crown-to-rump length (Stage 23).

The affected level and extension of the myeloschistic lesion were estimated from photographs or observation under binocular operative microscope (Fig. 1). The estimate was presented not in terms of the exact somite or vertebral segment number, but in more general terms, such as "low or high sacral cord," and "low, middle, or high lumbar cord." The coccygeal cord was included in the "low sacral cord" group. These neural openings were subdivided into "diffuse" and "localized" myeloschisis (Fig. 1). There were 12 embryos with diffuse myeloschisis, and in six of these, the whole neural tube was laid open. In the remaining six embryos, the rostral neural tube (the prosencephalon and/or the mesencephalon) was closed. An excessive amount of neural tissue (neural overgrowth) appeared to be present in the older embryos as shown in Fig. 2 right, but it was not apparent in the early, Stage 11, embryos (Fig. 2 left and center). There was one fetus with a crown-to-rump length of 140 mm, in which the whole neural tube was laid open. In this fetus, the neural overgrowth was not present (Fig. 3 upper left). Microscopically, the myeloschistic lesion of the embryos was that of a normal neural plate which had simply been left open (Fig. 2 center).

Localized Myeloschisis

Myeloschisis was found in the cervical or caudal areas, or in both. There were 20 embryos with cervical, and 57 with caudal myeloschisis. In the three embryos with combined locations, the areas of myeloschisis
were independent of each other (Figs. 1 and 4).

Cervical Myeloschisis. Cervical myeloschisis was invariably associated with neural opening in the low rhombencephalon, and the lesion often extended to the mesencephalon, or even to the prosencephalon (Figs. 1 and 5 left and right). Marked neural overgrowth was the rule in these lesions (Fig. 5), and it was already apparent in the smallest embryo at Stage 13. However, the overgrowth was not seen in the fetus with cervical myeloschisis (Fig. 3 upper right). Microscopically, cellular orientation (the cellular arrangement in relation to each other and their basic pattern in terms of the neural canal) was not much disturbed in the lesion. Their ventricles were smaller than normal,
and the primitive subarachnoid space over the prosencephalon seemed poorly developed. The primitive subarachnoid space around the spinal cord was well developed, and it was much more expanded in the region ventral to the everted neural plate (Fig. 5 center).

**Caudal Myeloschisis.** The lesion of caudal myeloschisis was found anywhere below the thoracic level (Fig. 1). A commonly affected site was the lumbar and sacral cord. In 18 embryos, the lesion was confined in the sacral or the sacrococcygeal cord (Figs. 1 and 6 lower right). All the lesions of this type showed an everted, barely exposed neural plate (Fig. 6). In most of them, there was an excessive amount of neural tissue even on gross inspection. The lesion was already apparent in the smallest embryo in Stage 12 (Fig. 6 upper left and center). Such neural overgrowth was limited in the dysraphic lesion, and other parts of the spinal cord were not affected. Some embryos revealed marked infolding of the cerebral wall suggestive of neural overgrowth, but in these embryos disintegration of various degrees was always observed. The everted neural plate retained its basic cellular orientation and most of the membrane covering the neural tissue (the external and internal membrane of Lemire, et al.28).

In one embryo with caudal myeloschisis, the everted neural plate was separated into the two independent parts, but the separation was considered to be artifact, since the evidence of traumatic insult was apparent. Duplication or trifurcation of the central canal was sometimes observed in the coccygeal cord caudal to the myeloschistic lesion, but it was not found in the rostral spinal cord. Duplication of the notochord was found in only one embryo. The cerebrospinal fluid pathway had developed normally in the embryos with caudal myeloschisis. There was no histological abnormality in their choroid plexus, the roof of the fourth ventricle, and the perineural primitive subarachnoid space, except that the primitive subarachnoid space ventral to the everted neural plate was much widened. No embryo revealed signs of hydrocephalus as represented by an enlarged head. Similarly, there was no enlargement of the central canal (syringomyelia or hydromyelia) (Fig. 6 upper right and lower left).
FIG. 3. Myeloschistic fetuses. Upper Left: Dorsal view of a fetus with diffuse myeloschisis, at crown-to-rump length of 140 mm. The neural tube is open in the spinal cord as well as in the more rostral part of the nervous system. Upper Right: Dorsal view of fetus No. 34633 with anencephaly and cervical myeloschisis, at crown-to-rump length of 170 mm. The dysraphic lesion involves the whole brain, cerebellum, and cervical cord as well as the upper thoracic cord. Lower Left: Dorsal view of fetus No. 37383 with thoracolumbar myeloschisis, at crown-to-rump length of 210 mm. A severe Arnold-Chiari malformation is seen. Lower Right: Conray ventriculography of fetus No. 37383 reveals apparent ventricular dilatation.
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Apparent dilatation of the lateral ventricles was found only in a myeloschistic fetus with a crown-to-rump length of 210 mm (Fig. 3 lower).

Holoprosencephaly

The complication of holoprosencephaly was found in 18 of the 92 myeloschistic embryos. The diagnosis of embryonic holoprosencephaly was based mainly on the characteristic facial anomalies (cyclopia, proboscis, or hypotelorism) as shown in Fig. 4, supplemented by disturbed diverticulation of the prosencephalon, which may be seen through the thin scalp under strong light.45

Arnold-Chiari Malformation

Arnold-Chiari malformation (downward herniation of the cerebellum into the cervical canal) was not present in any of our myeloschistic embryos. The cerebellum was not yet well developed, and its primordium was located in the upper portion of the fourth ventricle. The fourth ventricle was not herniated down into the cervical canal. However, Arnold-Chiari malformation was well developed in our two fetuses with lumbosacral myeloschisis of 176 mm and 210 mm crown-to-rump length (Fig. 3 lower left). In these fetuses, the angle between the spinal nerves and the spinal cord was studied according to the method of Barry, et al.\textsuperscript{1} The angle was broader just above the myeloschistic lesion, but it was normal in the upper thoracic level, implying that the traction force from the fixed myeloschistic cord is dissipated within the thoracic level.

Discussion

When compared with myelomeningocele after birth, embryonic myelomeningocele

![Fig. 4. Holoprosencephaly found in a myeloschistic embryo. Left: The face of embryo No. 21973 with holoprosencephaly and myeloschisis, at Stage 17. Interorbital distance is much narrowed. Note the proboscis (small arrow), and the prominent frontal bulging due to the unseparated telencephalic vesicle (large arrow). This embryo has two independent neural openings in the spinal cord, the cervical myeloschisis shown by two arrowheads and the lumbosacral myeloschisis shown (right). Right: The myeloschistic lesion, showing that the low lumbar and sacral cord are involved.](image)
FiG. 5. Embryos with cervical myeloschisis. Left: Dorsolateral view of embryo No. 10033 at Stage 15. The rhombencephalon and the cervical cord are widely everted and exposed. Center: Transverse section of the cervical cord of embryo No. 10033. The junction between the skin ectoderm and the edge of the everted neural plate is smooth. The primitive subarachnoid space ventral to the everted neural plate is much widened. The notochord (arrow) looks normal. H & E, × 36. Right: Lateral view of embryo No. 4972 at Stage 20. Neural opening is present in the mesencephalon and rhombencephalon, in addition to the cervical cord. An enormous neural overgrowth is present.

(myeloschisis) is different in several features. In the embryos, 1) dysraphic lesion is often more extensive; 2) the cervical cord is more frequently affected; 3) holoprosencephaly is frequently associated; 4) apparent hydrocephalus is not seen; and 5) meningocele is not found. These features characteristic of embryonic myeloschisis will be discussed.

Dysraphic Lesion

Diffuse myeloschisis involving the whole or almost all the neural tube was found in 15% of the present series. Such embryos should be extruded before birth by spontaneous abortion.

Involvement of Cervical Cord

The cervical cord was involved in 29% of the embryos with localized myeloschisis, whereas in only 4% of Matson’s series was spina bifida cystica situated there. A more important difference was that the lesions located in the cervical area of infants were usually skin-covered meningocele, often involving only two or three segments, without neurological deficit, whereas the embryonic lesion consisted of the exposed and widely everted neural plate, and was always associated with concomitant involvement of the rhombencephalon. The first fusion of the neural fold takes place at the site of the third or fourth somite (future lower occipital bone at the level of the lower rhombencephalon). This region seems vulnerable to dysraphic lesions, and cervical myeloschisis seems to be the extension of a low rhombencephalic lesion. With involvement of the region vital to life, most of these embryos would terminate in spontaneous abortions or be stillborn.

Associated Holoprosencephaly

Frequent association of holoprosencephaly is an unexpected finding. Holoprosencephaly is a grave malformation resulting from impairment of the prosencephalic diverticulation. The entity is exemplified by undeveloped or malformed cleavage of the
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Fig. 6. Embryos with caudal myeloschisis. Upper Left: Dorsal view of embryo No. 6390 at Stage 12, crown-to-rump length of 2.25 mm. The neural opening (arrow) is present in the thoracolumbar region. The lesion is regular in outline and has a linear median groove in the central region. Neural overgrowth is present. Upper Center: Photomicrograph of the myeloschistic lesion of embryo No. 6390. The tissue reveals disintegrative change of moderate degree. Unfortunately, the plane of the section is not exactly transverse to the spinal cord, and the spread of the excessive neural tissue seems to be more on the right side. The everted neural plate is surrounded by the external and internal limiting membranes. The cellular orientation is not much disturbed. This embryo is presented in more detail elsewhere. Azan, × 120. Upper Right: Lateral view of embryo No. 18289 with lumbosacral myeloschisis, at Stage 20. Arrow points to the dysraphic lesion. The head is of normal size. Lower Left: Caudodorsal view of the same myeloschistic lesion of embryo No. 18289. Arrow points to the opening of the central canal. Neural overgrowth is apparent. Lower Center: Photomicrograph of myeloschistic lesion of embryo No. 18289, transverse section. The neural plate is widely everted with neural overgrowth. The ventral primitive subarachnoid space is much widened. In this embryo, no abnormality is found in the histological appearance of the choroid plexus, the roof of the fourth ventricle, and the perineural primitive subarachnoid space except for the area ventral to the lesion. H & E, × 27. Lower Right: Dorsal view of embryo No. 7728 with sacrococcygeal myeloschisis, at Stage 16. Its histological features are essentially similar to those of lumbar myeloschisis.

cerebrum into the two hemispheres. It is often accompanied by various facial anomalies ranging from cyclopia to hypotelorism.8,22,40,43

Holoprosencephaly is a rare entity in infants,8 but it was one of the most common

malformations in our series of embryos (more common than myeloschisis).48,58 The prevalence of holoprosencephaly was 70 to 100 times higher in embryos than reported in newborn Japanese (the prevalence as reported ap-
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parently represents only those with characteristic facial dysmorphia), and it implies that almost all these embryos would be aborted. For this reason, association of myelomeningocele and holoprosencephaly is extremely rare in infants, although such cases are reported occasionally.

The tendency to extrude malformed embryos by spontaneous abortion is reported by other investigators. This tendency is also clearly shown by our findings that the ratio of spontaneous abortion is much higher in myeloschistic embryos than in our whole series of embryos (Table 1), and that many myeloschistic embryos have died in the uterus and were destined to be aborted later (Table 2). More severely malformed embryos would be more frequently extruded by abortion than the less malformed. Almost all holoprosencephalic embryos are extruded before birth, whereas about one out of 10 embryos with caudal myeloschisis (the embryonic forerunner of myelomeningocele) is retained to birth. Tanimura estimated from the present series that the prevalence of embryonic spina bifida was 0.27%, much higher than the 0.02% incidence of spina bifida cystica in newborn Japanese. The figure of 57 instances of caudal myeloschisis among 35,000 embryos does not represent the exact incidence, since the presence of the malformation might have been missed in some of the severely traumatized or dead embryos.

Hydrocephalus

Hydrocephalus was not present in our series of myeloschistic embryos, whereas it was found in one myeloschistic fetus. Diagnosis of embryonic hydrocephalus is difficult. In normal embryos, the ventricle becomes larger and the cerebral mantle becomes thinner in the late embryonic period. This stage of the normal embryo was called "physiological hydrocephalus" by Gardner. Our criterion of "abnormal" embryonic hydrocephalus is based on the head size, which seems apparently larger than the normal control on macroscopic observation. "Abnormal" hydrocephalus of the myeloschistic embryos may be masked by continuous drainage of cerebrospinal fluid through the myeloschistic neural opening. We believe, however, that the hydrocephalic process does not generally start before the latest embryonic stage. We noticed that hydrocephalus was absent in the holoprosencephalic embryos, whereas it is often found in holoprosencephalic fetuses and infants. In holoprosencephaly, there is no neural opening to remove excessive cerebrospinal fluid. Many embryos around developmental Stage 20 were found to have a strange outward bulge dorsal to the rhombencephalon, a feature reported as "nuchal blebs." If it were an expression of embryonic hydrocephalus (this possibility still remains to be proved), these would be the smallest embryos with hydrocephalus in our experience.

Meningocele

Meningocele (skin-covered outpouching of the dura mater) has not been found in our large series of embryos, nor has it been reported in the literature to our knowledge, although there should be no difficulty in finding such a malformation in embryos. At least five to six meningoceles would be expected among 57 embryos with caudal myeloschisis, since 10% to 20% of cases of "spina bifida cystica" in infants represent meningocele. The absence of meningocele implies that its first appearance is not at the embryonic stage, but is delayed to the fetal period. The dura mater may have to be separated from the spinal cord by the development of the subarachnoid space to produce the dural outpouching (meningocele). If so, appearance of meningocele is later than about Carnegie Stage 20, when the primitive subarachnoid space is formed in the dorsal spinal region.

Development of Myeloschisis

There are basically two contrasting theories regarding the development of a dysraphic lesion: 1) failure of the neural tube to close, and 2) rupture of the once-closed neural tube. Most teratologists and embryologists agree that myelomeningocele as well as anencephaly result from failure of closure rather than from rupture of the neural tube. But "rupture theory" is still persistently proposed by Gardner and Padget. The basic premise of the "rupture theory" is that the once-closed neural tube is re-opened by a hydrodynamic factor (abnormal increase of pressure within the closed
neural tube, resulting in hydrocephalus or hydromyelia). According to Gardner, this pressure increase is secondary to the thin roof of the fourth ventricle being impermeable to the passage of the cerebrospinal fluid. No abnormality was found, however, in the histological features of the roof of the fourth ventricle and the perineural primitive subarachnoid space in our myeloschistic embryos. Furthermore, myeloschisis is found in many early embryos before Stages 17 and 18, when cerebrospinal fluid begins to flow out from the fourth ventricle.

Padget proposes that “neuroschisis” (cleft formation in the dorsal neuroectoderm) is the embryonic forerunner of myelomeningocele and anencephaly. According to her, “neuroschisis” is formed by the rupture of the neural canal, and cerebrospinal fluid being pushed into the subectodermal space. Thereafter, the ectoderm is also ruptured to expose the nervous tissue. We sometimes observed Padget’s “neuroschisis” in our myeloschistic as well as normal human embryos. In our observation, a neuroschistic lesion is usually limited in area to two or three somites, and is not associated with eversion and overgrowth of the affected neural tube. Furthermore, there always remains the possibility that the neuroschistic lesion might be the artifact caused by operative or other manipulations. The rupture theory proposed by both Gardner and Padget is based on the assumption that hydrocephalus is present in the embryonic period, but we have not yet been able to find hydrocephalus in human embryos.

Our present evidence indicates that myelomeningocele is the result of disturbed closure of the neural plate, at least in most of the cases. Diffuse dysraphism in early embryos at Stage 11 cannot be the result of “reopening” since the embryos are still at the developmental stage when the neural tube closure is not yet completed in normal embryos. Diffuse dysraphism in older embryos and fetuses would not be induced by “reopening” either, because pressure within the neural tube would immediately be dissipated by rupture of the very limited portion involved. A similarly localized neural opening would evolve from the neural plate which failed to close, and there is little histological evidence to imply “rupture” of the neural tube in our early embryos with myeloschisis. This is especially seen in one myeloschistic embryo, No. 6390, which was in the posterior neuropore stage when the posterior neuropore was closing, the lesion was undoubtedly the result of non-closure.

Overgrowth of the neural tissue is almost always present in lesions seen in embryos. Similarly, Patten noticed an excessive amount of neural tissue in the myeloschistic lesion as well as in the rostral neural tube. Although severe infolding of the rostral neural wall is dismissed as artifact by Sjödin, the overgrowth in myeloschistic lesions has been regarded as non-artefactual by many other investigators. However, it is still debatable whether the overgrowth is the cause, or just the secondary phenomenon of non-closure. Defective limiting membrane or somite necrosis have been implicated as causes of non-closure; however, there is no evidence supporting these hypotheses in our series, and the factor that inhibits neural tube closure remains unknown.

Impairment of the recanalization of the caudal spinal cord is often associated with this malformation. The site of posterior neuropore closure is estimated to be at the level of L-1 or L-2, with probable variation of not more than two segments rostral or caudal (that is, T1-L4). The more caudal spinal cord is considered to be formed by recanalization of the caudal cell mass. Myeloschisis in the thoracolumbar region frequently extends into the sacral cord. Furthermore, myeloschisis is often limited in the sacral spinal cord. These lesions should theoretically be attributed not to non-closure of the neural plate, but to disturbance of the recanalization process of the caudal cell mass.

The term “spina bifida cystica” includes both meningocele covered by the skin, and myelomeningocele with exposed neural tissue. The two malformations are generally considered to represent different degrees of severity of an entity of the same pathogenesis. But our observation implies that they are entities of different pathogenesis, appearing at different developmental stages. Myelomeningocele is formed in the early embryonic period by non-closure of the neural tube or possibly by disturbance of the recanalization process, whereas meningocele is formed probably in the early fetal period by a mechanism presently unknown. There is little possibility that meningocele is formed by sub-
sequent coverage of the open neural plate by the dura and skin, since such a repair process is not seen in older embryos and fetuses with myeloschisis. A hydrodynamic factor may be considered for the formation of meningocele. Arnold-Chiari malformation is formed in the early fetal period. For the mechanism of its formation, various theories have been proposed.\(^5,10,13,14,19,36,30,49\) Our present study confirms the report of Barry, et al.,\(^1\) that traction force from below is dissipated in the upper thoracic level, and that development of the Arnold-Chiari malformation cannot be explained by traction theory.

Acknowledgment

The authors are deeply indebted to Dr. Osamu Tanaka, Associate Professor at the Human Embryo Center for Teratological Studies, for his generous permission to study the collection of the human embryos in the Center.

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