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M Sarwar, C Virapongse and S Bhimani

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Primary Tethered Cord Syndrome: A New Hypothesis of Its Origin

Mohammad Sarwar[1]
Chat Virapongse
Sultan Bhimani

Primary tethered cord syndrome is defined as low placement of the spinal cord and thickened filum terminale with associated anomalies. This definition excludes anomalies concomitant with overt myelomeningocele and spinal cord tethering secondary to myelomeningocele repair. Embryologically, the primary tethered cord syndrome is an entirely different entity from overt myelomeningocele and associated Arnold-Chiari type II malformation, but its origins have not been satisfactorily explained. The authors postulate that primary tethered cord syndrome is a manifestation of local dysmorphogenesis of all three germ layers at the lumbosacral area, possibly triggered by a hemorrhagic, inflammatory, or some other local lesion occurring in embryogenesis.

Primary tethered cord syndrome is poorly understood. Its embryology and pathogenesis have not been satisfactorily explained [1–3]. Little is known about the relation between spinal cord biomechanics and the neurologic deficit caused by the primary tethered cord syndrome. We review and reassess the data on this syndrome and offer a new hypothesis of its origin.

Primary tethered cord syndrome can be defined as low placement of the spinal cord and thickened filum terminale with associated anomalies (lipoma, but not lipomyeloschisis; epidermoid or dermoid; cord duplication or cord dysgenesis [4]; diastematomyelia [5]; and adhesions). Anomalies concomitant with overt myelomeningocele and spinal cord tethering secondary to myelomeningocele repair are excluded [6]. The syndrome is a form of occult spinal dysraphism that may be manifested by skin pigmentation or nevus, hairy patch, hypertrichosis, subcutaneous lipoma, or a dermal sinus tract. Generally accepted features of the syndrome include presentation at any age, although it is far more common in children; a clinical spectrum including pain, sensorimotor deficit, bladder and bowel dysfunction, leg atrophy, foot deformity, and scoliosis; demonstration by myelography, particularly metrizamide myelography complemented by metrizamide-enhanced computed tomography [7, 8]; and inconsistent improvement after surgery, with some symptoms improving more than others [9–11].

Any well defined syndrome or disease entity is characterized by a generally prevailing coherence among its clinical manifestations, pathologic characteristics, and therapeutic outcome in a majority of patients. Such is not the case in the primary tethered cord syndrome. As yet unexplained are (1) why this syndrome presents in different age groups; (2) why the clinical symptoms are significantly different in children than in adults [11]; (3) whether the low-lying spinal cord is pulled down by a relatively faster-growing and disproportionately longer spinal column; (4) why a thickened filum terminale causes traction in itself and in the lower spinal cord; and (5) why transection of the filum terminale is not uniformly efficacious. To address some of these uncertainties as well as the pathogenesis of the syndrome, we review spinal cord development and its relation to the spinal column; the biomechanical (viscoelastic) properties of the spinal cord; and the relevance of these factors to the primary tethered cord syndrome.

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[1] All authors: Department of Diagnostic Imaging, Section of Neuroradiology, Yale University School of Medicine, 333 Cedar St., New Haven, CT 06510. Address reprint requests to M. Sarwar.

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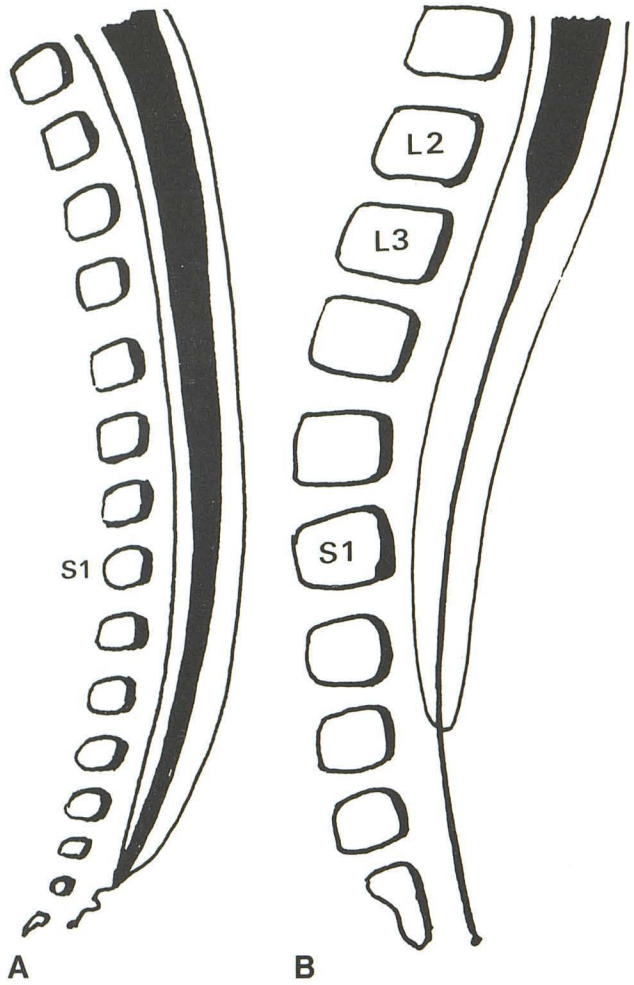

Fig. 1.—Spinal column and cord at about 3 months of gestation (**A**); at birth (**B**). Spinal cord is at progressively higher level of spinal column during developmental period because of disproportionate rates of growth of column and cord.

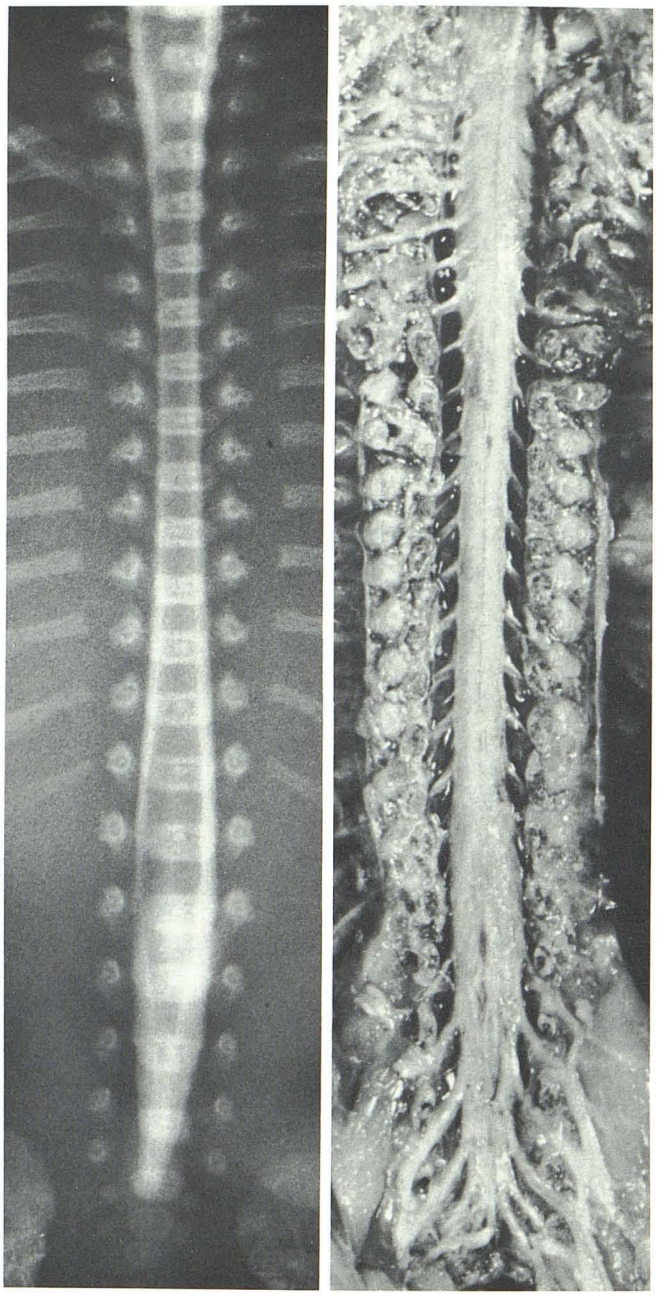

Fig. 2.—Conray myelogram in fetus. Spinal column and cord at 5–6 months of gestation. Cord ends at about L4 level.

Fig. 3.—Autopsy specimen of fetus. Normal nerve-root angulation at 30 weeks of gestation. Gradually progressive caudad angulation of nerve root from cervical to lumbar region. (Normally, such angulation is recognizable at 7 weeks gestation.) (Courtesy of Robert Shapiro.)

Normal Spinal Cord Development and Spinal Column Growth

Spinal cord development can be divided into three zones [12–14]: cranial, transitional, and caudal. The cranial zone develops in the classic manner, that is, by folding and closure of the neural tube to form the cervical and thoracic levels of the cord. The caudal zone develops from contributions by the pluripotent cells of the primitive streak and forms the conus (coccygeal) region of the cord. The transitional zone has features of both types of development and forms the lumbar and sacral levels of the cord.

At about 3 months of gestation, the spinal cord covers the entire length of the spinal column (down to coccyx 2) (fig. 1A). At 5 months of gestation, the top of the spinal cord is located at about S1 level; at 6 months of gestation, it is at the level of the L3–L4 vertebrae (fig. 2); and at birth, it reaches L2–L3 level (fig. 1B). In an adult, the conus medullaris lies at L1–L2 level [15]. The spinal ganglia are derived from the neural crest cells at about 25–30 days of gestation. They connect with the spinal cord and the spinal nerves by about 38 days of gestation. At about the same time, the meninx primitiva, which is of mesodermal origin and gives rise to meninges, surrounds the neural tube [16, 17]. By about 50–55 days of gestation, the cord is completely invested with dura mater. Compared with the development of the cord, vertebral column development proceeds at a somewhat slower pace. The spinal column

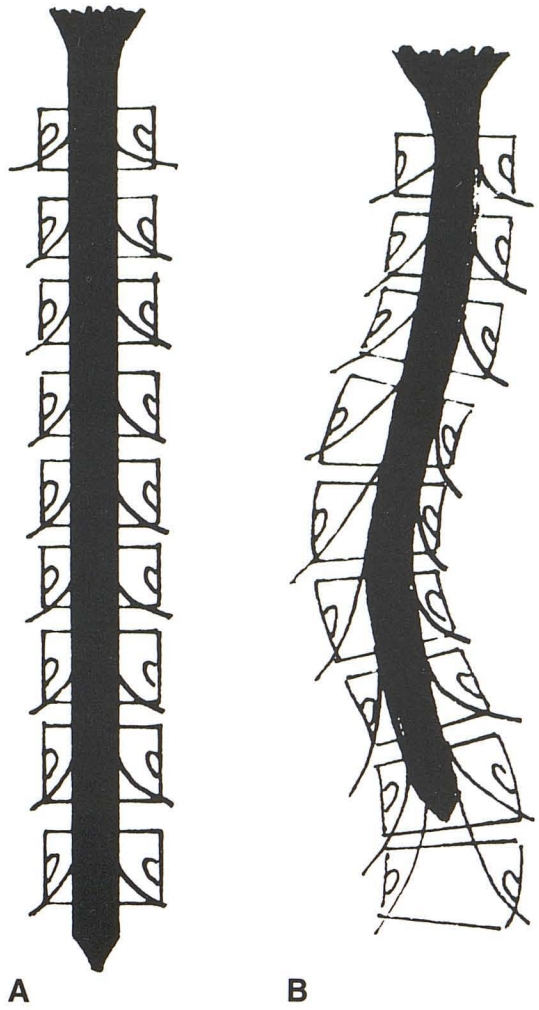

Fig. 4.—**A**, Normal spinal cord–column relation; **B**, distortion (scoliosis) of spinal column in attempt to accommodate to shorter cord. (Adapted from [22].)

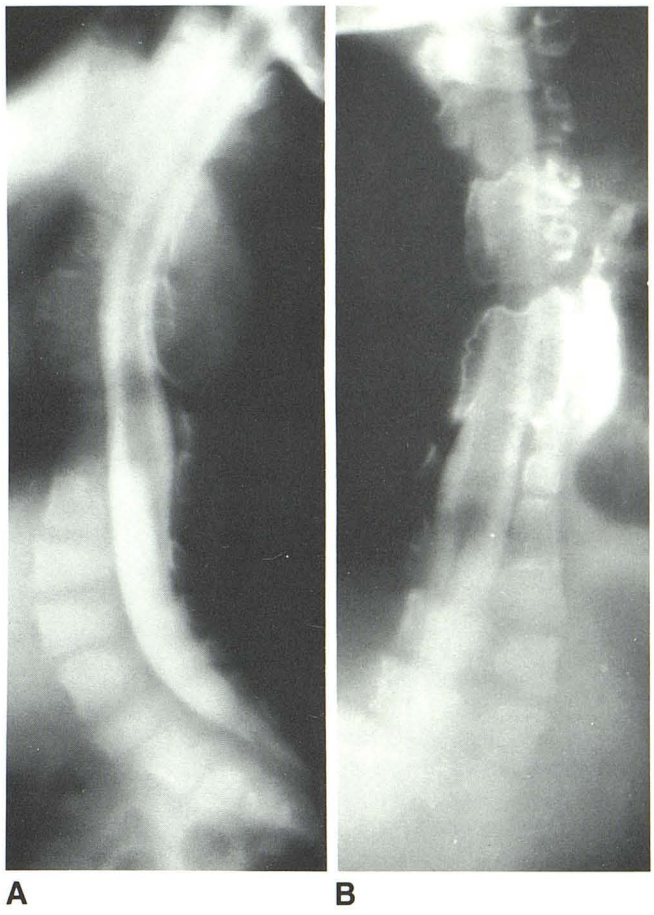

Fig. 5.—Short spinal cord and spine dysmorphogenesis in 6-year-old boy with Jarcho-Levin syndrome (spondylothoracic dysostosis). Lateral (**A**) and anteroposterior (**B**) polytomograms obtained at metrizamide myelography. Cord was only 18 cm long; it should have attained almost adult length (42–45 cm) at this age. Short spinal cord probably led to adaptive spinal column dysmorphogenesis. Cervicolumbar spine had only 20 or 21 segments instead of normal 24. Except for "crablike" rib deformity, believed related to spine segmentation anomaly, no other skeletal dysplasia was present.

is still at the membranous stage until about 40 days of gestation and at the chondrification stage up to 55–60 days of gestation [16].

Like the relation between growth of the brain and the calvarium, the growth and form of the spinal column is influenced by growth of the spinal cord [18–20]. The spinal column has inherent potential for longitudinal growth, which is modified by development of the contained neural tissue and angulation of the emerging spinal nerve roots. In the early embryo, the nerve roots are oriented horizontally. Their angulation becomes recognizable at about 7 weeks of gestation (fig. 3). The traditional view is that such angulation is influenced by somewhat faster longitudinal growth of the spinal column. According to Roth [21], however, the reverse is more likely. He theorizes that the nerve-root angulation occurs during the early weeks of development by a process called "growth by neural extension." This type of neural growth is characterized by the formation of processes several centimeters long from a single cell body. According to Roth, then, "the growth in length of the vertebral column depends upon the growth in length potential of the cord–nerve root complex" [22]. In other words, the spinal column may be expected to become distorted (scoliotic) [22] (fig. 4) or dysmorphogenetic (fig. 5) as it adjusts itself to a cord that is shorter than normal.

The gradual increase in obliquity of the spinal nerves from the cervical to the lumbosacral cord explains the corresponding increase in the interpedicular height (fig. 6). This pedicle–nerve root relation bears out the influence the nerve-root angulation has on spinal morphology. Any disease process that impairs the normal nerve-root angulation is expected to modify interpedicular height accordingly (fig. 7).

Biomechanics of the Spinal Cord

Although the spinal cord is considered a viscoelastic structure, little information is available on its biomechanics. Breig [23, 24], who investigated the biomechanics of the central nervous system in cadavers, studied the deformation of the

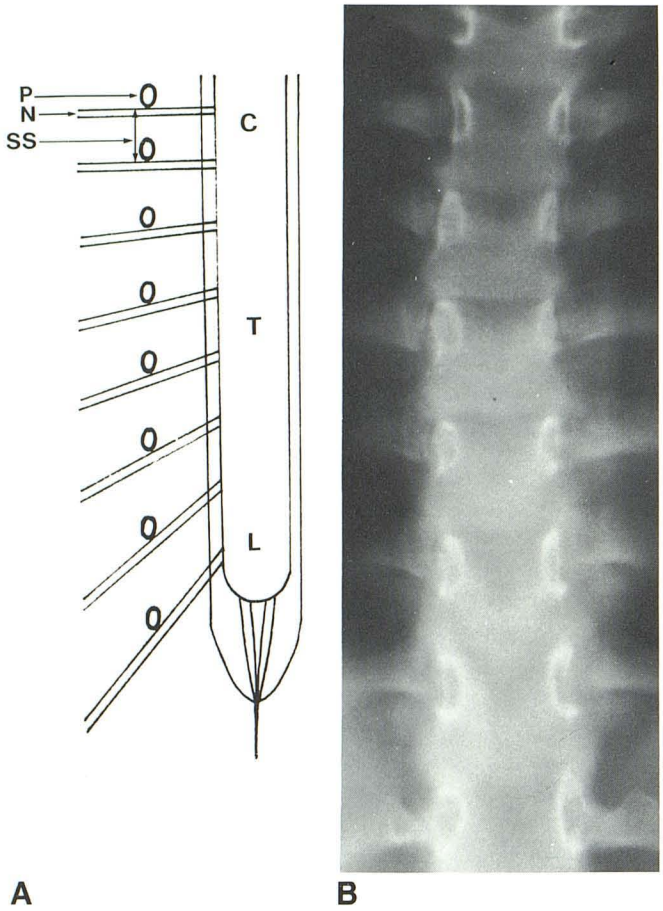

Fig. 6.—**A**, Spinal segment (SS) is distance between inferior aspects of adjacent pedicles (P) and also defines distance between neighboring nerve roots (N). As nerve roots become more oblique caudad, spinal segments increase in height. Any lesion that lessens nerve-root obliquity will result in diminution of spinal segment height. C = cervical; T = thoracic; L = lumbar. **B**, Tomogram in normal 6-year-old boy. Progressive increase in height of spinal segments from cephalad to caudad.

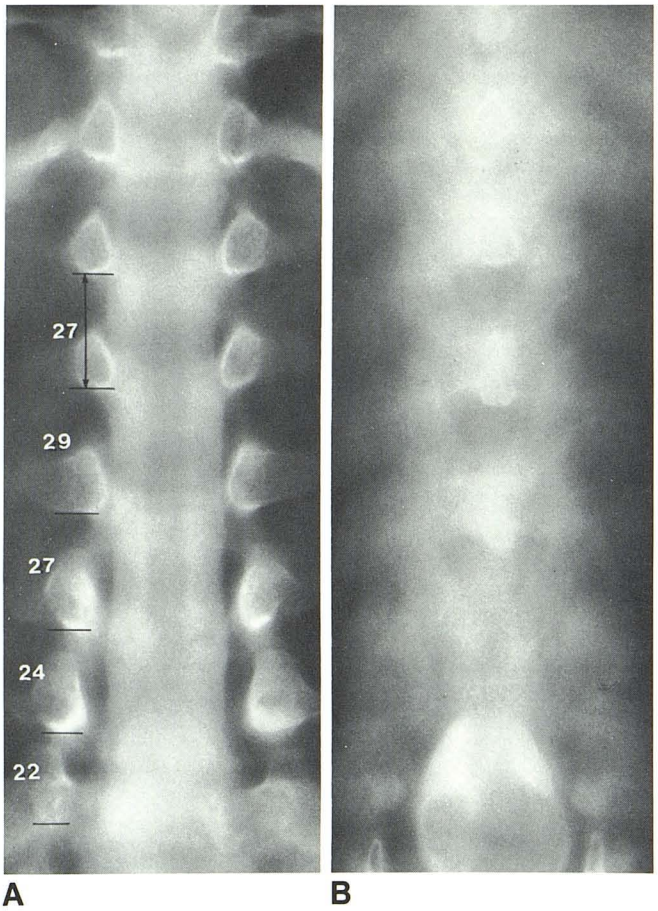

Fig. 7.—**A** and **B**, Tethered cord and intradural lipoma in 5-year-old boy. Lumbar spinal segment height diminishes caudad. Normally, spinal segment height increases gradually from cervical region to about L4 level. Values represent height in millimeters.

brainstem and spinal cord, especially the cervical cord, during bending of the spine in four directions. He established the dynamism of the spinal cord and noted elongation of the cervical cord in flexion and its slackening in extension. He showed that in the neutral position, the cord folds like an accordion and is under slight tension. During flexion, the spinal cord first unfolds, then undergoes elastic deformation near full flexion; during extension, it first folds, then undergoes some elastic compression. The change in length measured on its dorsal aspect in flexion and extension was 1.8–2.8 cm for the cervical cord, 0.9–1.3 cm for the thoracic cord, and 1–2 cm for the lumbar cord. On lateral flexion of the cervical spine, the convex aspect of the cord was elongated by about 6 mm and the concave aspect correspondingly shortened. At myelography, Breig showed the lumbar nerve root stretching and slackening during flexion and extension, respectively, of the cervical spine.

Barry et al. [25] demonstrated that the thoracic cord segments were abnormally long in a fetus with lower thoracic myeloschisis, while in another fetus with lower lumbar myeloschisis, the lumbar cord segments were abnormally long. They stated that such segmental cord lengthening resulted from caudad traction induced by the cord anomaly. In these fetuses, the spinal cord elongation was maximal adjacent to the anomaly and became progressively less marked distad. Smith [26] used posture in monkeys to show radiographic changes in length and position of spinal cord segments.

Sarwar et al. [27] measured cord elongation in fresh human fetuses and in animals. They exposed the cord by total laminectomy in the fetuses and by three-level (cervical, thoracic, lumbar) laminectomy in the animals. Cord elongation was created by application of forceps and weights. The cord lengthening at the midcervical, midthoracic, and lumbar levels was measured by observing displacement of a suture applied over the cord in reference to pins placed in the soft tissue at matching levels. They noted that after a variable lag period, the cord elongation was roughly proportional to the magnitude of the applied force until the point of maximal stretchability was reached—at which point the cord ceased to elongate any further, but did not break. The cord was shown to stretch most in the lumbar region, slightly in the thoracic region, and minimally to not at all in the cervical region (fig. 8). Elasticity

of the cord tissue was demonstrated by its ability to regain its original position at each level upon cessation of traction.

Relevance of Developmental and Biomechanical Factors to Primary Tethered Cord Syndrome

Morphologic Features

Abnormally low placement of the spinal cord. In the primary tethered cord syndrome, the spinal cord usually lies at or below L2–L3 level. Temporarily disregarding the effect of traction on cord length, one may ask whether the spinal cord in this syndrome is abnormally long (normal average length: 45 cm) and the spinal column of normal length (normal average length: 75 cm) or, conversely, the spinal cord is of normal length and spinal column abnormally short. Unfortunately, no studies have been conducted on this subject. However, our clinical experience has provided no evidence that the spinal column is abnormally short in the primary tethered cord syndrome. Moreover, it does not seem logical to assume that a cord abnormally long per se should be abnormally stretched. Logically, abnormal elongation of the cord should be caused by either pull from below or push from above. Let us consider the situation at the caudal and cephalic ends of the cord.

Thickening of the filum terminale and anomalies at the termination of the cord. The normal filum terminale is a delicate structure, 20 cm long and usually less than 2 mm thick. Neural tissue is present only in its proximal 5 cm; the rest consists of connective tissue. Its proximal 5–6 mm also contains the central canal. The upper 15 cm of the filum terminale is within the thecal sac, the rest outside the dura. It is attached to the dorsal aspect of the first coccygeal segment. The filum terminale develops by initial dedifferentiation into a fibrous strand of the spinal cord caudal to the second coccygeal segment. This fibrous strand then elongates by interstitial growth to adapt itself to the lengthening spinal column (and receding level of the spinal cord) [28].

By definition, the filum terminale in the primary tethered cord syndrome is more than 2 mm thick. The thick filum terminale may also include fibrolipomatous infiltration and, rarely, abnormal extension of the dilated central canal [29]. Logically, the normal or abnormal filum terminale alone can cause traction only if it has undergone a reduction in length at some stage of development or if the spinal column lengthens disproportionately, thus dragging the filum terminale caudad with it. However, no published accounts are available to clarify this aspect of the primary tethered cord syndrome. It seems reasonable to state that an imbalance must exist in the rate of growth of the neuroectodermal (neural tissue, spinal cord, nerve roots) and mesodermal (spine, spinal cord coverings) derivatives to produce stretching of the lumbosacral cord. If the spinal column growth rate is not slower than that of the spinal cord, there must be some abnormal stretch-producing mechanism between the neural tissue and the mesenchyme to account for the low-lying cord, as will be discussed. We postulate this mechanism to be the adhesions or other anomalies found in the primary tethered cord syndrome. As most of the adhesions and anomalies lie within the distal thecal sac, their contraction produces traction on the cord.

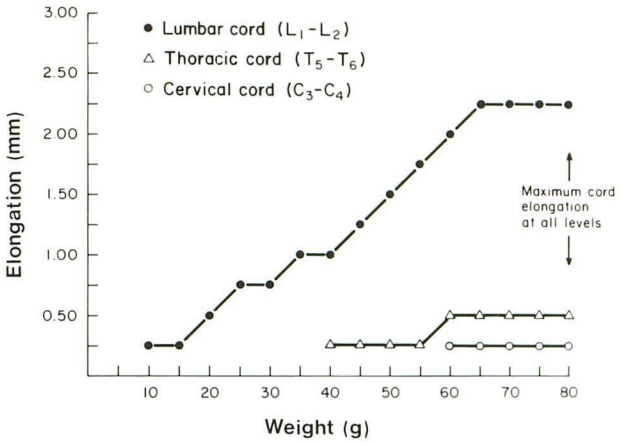

Fig. 8.—Spinal cord elongation in fetus with graduated application of weights. After a lag period, lumbar cord elongation is roughly proportional to magnitude of applied force until maximum stretchability is reached. There is a longer lag period after beginning of weight application in thoracic cord, and cord elongation that follows is slight. No cervical cord elongation is noted. (Reprinted from [27].)

Nerve root angulation and Arnold-Chiari malformation. The caudal nerve roots in this anomaly do not exhibit their normal downward oblique course; rather, they pursue a horizontal or even an upward-slanting course. Such a change in nerve-root angulation has been suggested erroneously as a cause of Arnold-Chiari type II malformation in patients with myelomeningocele. Barry et al. [25] demonstrated conclusively in fetuses with myeloschisis that such a change in nerve-root angulation dissipates within five segments cephalad from the anomaly. Goldstein and Kepes [30] tethered the cord experimentally in 500 newborn rats and 207 opossum fetuses by crushing the spine and the spinal cord at L4–L5 level. In eight rats and 16 opossum fetuses that survived to adulthood, the cord remained at the crushed level, indicating that spine and spinal cord grew as a unit from intermingling of the mesoderm and neuroectoderm. Neither change in angulation of the proximal cervical nerve roots nor caudal descent of the cerebellum or brainstem was noted. They concluded that traction by tethered cord does not cause Arnold-Chiari malformation.

Sarwar et al. [27] have shown that forceps traction at the cauda equina in human fresh fetuses also causes maximal lumbosacral cord elongation, and minimal to no elongation occurs in the cervical cord. In other words, traction at the cauda equina affects mainly the lumbosacral cord. This observation is further supported clinically by the fact that Arnold-Chiari malformation is seen seldom, if at all, in association with the primary tethered cord syndrome. Of 32 cases of occult spinal dysraphism studied myelographically by Gryspeerdt [31], none had concurrent Arnold-Chiari malformation. Of 34 cases of childhood diastematomyelia reported by Hilal et al. [5], none had concurrent Arnold-Chiari malformation. Of 14 cases of lipomyeloschisis recently recorded by Naidich et al. [32], only one had concomitant Arnold-Chiari malformation. Embryologically, Arnold-Chiari malformation antedates the

primary tethered cord syndrome; the former is recognizable at about 6–8 weeks of gestation, whereas the latter is manifest at about 8–10 weeks of gestation or later. In Arnold-Chiari malformation, the course of only the most proximal cervical nerve roots is altered (from horizontal to upward-slanting). This is caused by downward pressure on the proximal cervical cord by the low-lying cerebellar and brainstem hernia.

Clinical Symptoms

The investigations of Barry et al. [25], Reimann et al. [15], Emery and Naik [33, 34], and Sarwar et al. [27] have shown that in clinical and experimental cases of cord tethering, the maximal elongation occurs in the lumbosacral cord. The confinement of stretch to the lumbosacral cord may suggest a bracing action of the dentate ligaments in the lumbar region, as seen in the cervical region [33]. These observations are concordant with the pathophysiologic changes of the lumbosacral cord in the primary tethered cord syndrome, shown by Yamada et al. [35]. These investigators studied the oxidative metabolic functioning and electrophysiologic changes in this anomaly and concluded that "symptoms and signs of tethered cord syndrome are concomitant with lumbosacral neuronal dysfunction which could be due to impairment of mitochondrial oxidative metabolism under constant or intermittent cord stretching" [35]. Such metabolic changes are probably attributable to stretching with distortion of vascular structures. These authors showed that untethering improves oxidative metabolism and possibly facilitates neuronal reparative mechanisms.

The degree of clinical neurologic deficit, in the syndrome and the surgical outcome [9–11] probably are related to (1) tolerance to stretch of the neural tissue in each individual, (2) locomotion (neck flexion stretches lumbar nerve roots and can exacerbate pain in primary tethered cord patients), and (3) the length of time the cord has been subjected to the abnormal stretching. It is likely that different groups of neurons or tracts respond differently to stretch. For example, the fact that sphincter function is least likely to improve after untethering may suggest increased vulnerability to stretch of the neurons and fiber tracts involved in micturition control. Presumably, if the stretch-induced neural tissue damage is extensive or irreversible, amelioration of neurologic deficit after untethering will be minimal to none. Logically, then, the sooner the untethering procedure is performed, the more likely repair will be satisfactory.

Discussion

From the foregoing, it is apparent that experimental observations on mechanical deformation of the cord theoretically can explain the lumbosacral symptoms in the primary tethered cord syndrome. The major void is an explanation for its pathogenesis. One possible embryologic explanation of low-lying cord can be found in the development of the filum terminale [28]. Since filum terminale forms by dedifferentiation of the caudal cord, the absence of such dedifferentiation might result in a longer and therefore lower cord than normal. If this were the case, however, there would be no reason for cord traction nor any explanation for the associated lesions.

The principal error in describing the primary tethered cord syndrome has been the concept of ascent of the cord. Many researchers mistakenly have ascribed the syndrome to failure of the cord to ascend. These investigators have failed to consider how filum terminale traction could occur if the cord has not ascended. The only way cord traction can occur is through an altered growth relation between the spinal column–spinal cord complex or some other mechanism whereby the cord is pulled down.

Previous reports have not dealt with the question of an impaired growth pattern of the spinal column–spinal cord complex, nor does our own experience suggest such an altered relation in this syndrome. The only other plausible explanation lies in the other lesions that may exert traction on the cord. Such "traction" lesions include (1) intradural lumbosacral lipoma, alone or in contiguity with cord [31] or filum terminale; (2) thickened and fibrotic filum terminale with or without associated lipoma; (3) diastematomyelia (cord lies below L2 level in 76% of cases [5]) associated with aberrant bands or dorsal roots extending to (27%) and through the dura (45%) [1, 36–39]; and (4) simple bands, dermal sinus, coccygeal cyst, and meningocele manque (atretic meningocele containing recurrent nerve roots or spinal cord segment). Such traction lesions were present in 66 of 100 cases reported by James and Lassman [1], 27 of 31 cases reported by Hoffman et al. [9], and all 31 cases reported by Pang and Wilberger [11] (excluding their one case of postmyelomeningocele repair). In all 16 cases of thickened filum terminale in the series of Pang and Wilberger, excised filum terminale segments uniformly revealed fibrofatty tissue with occasional nests of ependymal calls.

These observations strongly support the tethering effect of such lesions. The tethering must have resulted from contraction of an elastic tissue of which the fibrofatty tissue is residual evidence. The concept of tight filum terminale causing traction is very tenuous. Indeed, cutting the normal filum terminale causes it to curl on itself without affecting the cord position [27]. In only five of 100 primary tethered cord cases did James and Lassman [1] find tight filum terminale, and they rightly questioned the existence of this as a clinical entity per se.

If the so-called traction lesions play a major role in the morphogeneis of the primary tethered cord syndrome, how do we explain their origin? Before discussing this, we must note that caudal dislocation of the cord in this syndrome is not on the same basis as in overt myelomeningocele and associated Arnold-Chiari type II malformation. In overt myelomeningocele, the cord and nerve roots are within the dural sac. Their embryogenesis, as suggested by Gardner [40, 41], entails rupture of a previously closed distended caudal neural tube (distal neuropore). The Arnold-Chiari type II malformation associated with myelomeningocele is not caused by traction caudad to the cord; rather, it stems from other poorly understood factors.

As for the primary tethered cord syndrome, we hypothesize that, as alluded to by Warkany et al. [42], some hemorrhagic, inflammatory, or other local insult to the caudal cord occurs

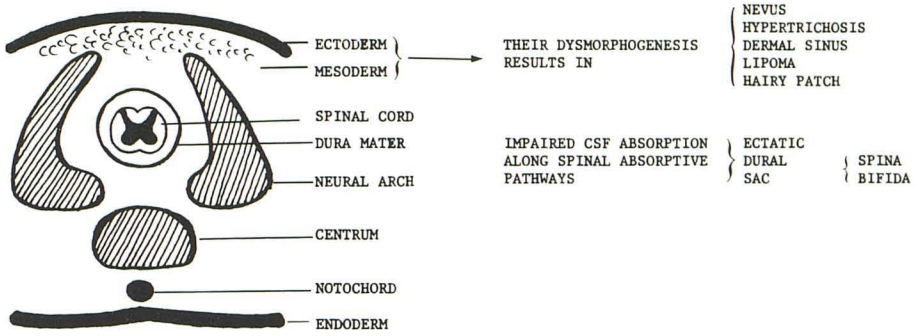

Fig. 9.—Hypothesis of developmental pathogenesis of associated lesions in primary tethered cord syndrome. Diagram depicts an early somite and sclerotome.

in late embryogenesis or early fetal life before the mesodermal spinal column has assumed any definitive form. This results in the reparative evolution of elastic or fibrofatty bands, which may form aggregated clumps or long columns to present as we know them postnatally at surgery. Their contraction during the healing process could tether the cord. If extradural adhesions were to develop as well, the disproportionately faster longitudinal growth rate of the spinal column, however temporary, might tether the cord further and exaggerate its stretching distortion.

The paucity of reported evidence for such extradural bands might be explained by their emerging with the "normal" epidural fibrofatty tissue. They may be sacrificed and thus escape recognition as distinct structures as the surgeon works through the epidural tissue to reach the dura. The work of Goldstein and Kepes [30] lends support to such a concept.

Although this hypothesis is compatible with the observed altered angulation of the nerve roots and the majority of associated anomalies, it fails to explain the ectatic dural sac, the unfused neural arches, and the cutaneous and subcutaneous lesions present in the primary tethered cord syndrome. We postulate that the lesion that causes the adhesions induces impairment of the local cerebrospinal fluid (CSF) absorptive pathways along the nerve roots [43–46]. The resultant ectatic thecal sac secondarily impedes convergence of the neural arches (spina bifida). The same theoretic pathogenetic lesion also triggers dysmorphogenesis of the adjoining ectodermal and mesodermal derivatives, resulting in the formation of the cutaneous and subcutaneous lesions seen in the syndrome (fig. 9). This concept embraces the mutually inductive influence of all three germ layers in early morphogenesis of the spinal cord and its surroundings, a viewpoint also expounded by Lichtenstein [47] in 1940. That local spinal dysraphism (myeloschisis) can be induced in chicken embryos by a dorsal midline incision of the caudal spine and recently closed neural tube has been demonstrated by Naidich et al. [32].

Overt spinal dysraphism (myelomeningocele) with associated Arnold-Chiari type II malformation is developmentally different from the primary tethered cord syndrome (occult spinal dysraphism). In overt spinal dysraphism, the distal neuropore remains open and the neural plate is flat. Many theories attempt to explain the associated Arnold-Chiari type II malformation. Cameron [48] theorizes that the CSF that escapes from the open distal neuropore into the amniotic sac produces aminotic fluid pressure that is greater than the intracranial pressure. This pressure differential squeezes the intracranial contents caudad, resulting in herniation of the lower brainstem and cerebellum through the foramen magnum. The CSF pulse wave acts through the hernia primarily on the dorsal aspect of the cervical cord rather than being dissipated uniformly along the entire spinal cord as is normal. Also, the cephalad-driving CSF pulse wave meets resistance at the brainstem and cerebellar hernia, adding further insult to the cervical cord. These dynamic factors [49] account for the high incidence of primarily dorsal syringomyelia seen in overt spinal dysraphism (myelomeningocele). In contrast, the primary tethered cord syndrome (occult dysraphism) seems to represent a local dysmorphogenesis of all three germ layers at the lumbosacral area, thus explaining why other cephalad anomalies (Arnold-Chiari malformation, syringomyelia) are not part of this entity. When present, they are probably coincidental.

Summary and Conclusions

The low placement of the cord and its tethering in the primary tethered cord syndrome have not been adequately explained embryologically. We postulate that a hemorrhagic, inflammatory, or some other local lesion of the caudal cord occurs in embryogenesis or early fetal life, producing the "other" lesions so commonly seen in this syndrome. These lesions exert traction on the developing cord.

The spinal cord is a viscoelastic tissue. Elongation occurs predominantly in the lumbosacral cord. This local deformation explains the lumbosacral cord dysfunction shown experimentally and observed clinically in the primary tethered cord syndrome. The altered angulation of the nerve roots being limited to the caudal nerve roots supports this premise. This property also indicates that traction from below is not the cause of downward herniation of the cerebellum and brainstem (Arnold-Chairi malformation). Developmentally, the primary tethered cord syndrome is an entirely different entity from overt myelomeningocele and associated Arnold-Chiari type II malformation, thus accounting for their nonassociation.

REFERENCES

1. James CCM, Lassman LP. Spinal dysraphism. London: Butterworth, **1972**:8–17
2. Kallen B. Early embryogenesis of the central nervous system with special reference to closure defects. *Dev Med Child Neurol [Suppl]* **1968**;16:44–53

3. Patten BM. Embryological stages in the establishing of myeloschisis with spina bifida. *Am J Anat* **1953**;93:365–395
4. Emery JL, Lendon RG. The local cord lesion in neurospinal dysraphism (meningomyelocele). *J Pathol* **1973**;110:83–96
5. Hilal SK, Marton D, Pollack E. Diastematomyelia in children. Radiographic study of 34 cases. *Radiology* **1974**;112:609–621
6. Heinz ER, Rosenbaum AE, Scarf TB, Reigel DH, Drayer BP. Tethered spinal cord following myelomeningocele repair. *Radiology* **1979**;131:153–160
7. Harwood-Nash DC. Computed tomography of the pediatric spine: A protocol for the 1980's. *Radiol Clin North Am* **1981**;19:479–494
8. Pettersson H, Harwood-Nash DCF. CT and myelography of the spine and cord. New York: Springer-Verlag, **1982**
9. Hoffman HJ, Hendrick EB, Humphreys RP. The tethered spinal cord: its protean manifestations, diagnosis and surgical correction. *Childs Brain* **1976**;2:145–155
10. Linder M, Rosenstein J, Sklar FH. Functional improvement after spinal surgery for the dysraphic malformation. *Neurosurgery* **1982**;11:622–624
11. Pang D, Wilberger JE. Tethered cord syndrome in adults. *J Neurosurg* **1982**;57:32–47
12. Angevine JB. Clinically relevant embryology of the vertebral column and spinal cord. *Clin Neurosurg* **1973**;20:95–113
13. Dryden RJ. Duplication of the spinal cord: a discussion of the possible embryogenesis of diplomyelia. *Dev Med Child Neurol* **1981**;22:234–243
14. Sarwar M, Kier EL, Virapongse C. Development of the spine and spinal cord. In: Newton TH, Potts DG, eds. *Modern neuroradiology*, vol 1. *Computed tomography of the spine and spinal cord*. San Francisco and New York: Clavadel, **1982**:15–30
15. Reimann AF, Anson BJ. Vertebral level of termination of the spinal cord with report of a case of sacral cord. *Anat Rec* **1944**;88:127–138
16. Lemire RJ, Loeser JD, Leech RW, Alvord EC. *Normal and abnormal development of the human nervous system*. Hagerstown, MD: Harper & Row, **1975**:282, 311
17. Sensenig EC. The early development of the human vertebral column. *Contrib Embryol* **1949**;33:21–62
18. Holtzer H. Experimental analysis of development of spinal column: I. Response of precartilage cells to size variations of spinal cord. *J Exp Zool* **1952**;121:121–147
19. Detwiler SR, Holtzer H. The inductive and formative influence of the spinal cord upon the vertebral column. *Bull Hosp Jt Dis Orthop Inst* **1954**;15:114–123
20. Holtzer H. An experimental analysis of the development of the spinal column: II. The dispensability of the notochord. *J Exp Zool* **1952**;121:573–592
21. Roth M. Normal neurovertebral relations. In: Shapiro R, ed. Myelography. Revised 4th ed. Chicago: Year Book Medical (in press)
22. Roth M. Idiopathic scoliosis from the point of view of the neuroradiologist. *Neuroradiology* **1981**;21:133–138
23. Breig A. Biomechanics of the central nervous system. Some basic normal and pathologic phenomena. Stockholm: Almqvist and Wiksell, **1960**
24. Breig A, El-Nadi AF. Biomechanics of the cervical spinal cord. *Acta Radiol [Diagn]* (Stockh) **1966**;4:602–624
25. Barry A, Patten BM, Steward BH. Possible factors in the development of the Arnold-Chiari malformation. *J Neurosurg* **1957**;14:285–301
26. Smith CG. Changes in length and position of the segments of the spinal cord with changes in posture in the monkey. *Radiology* **1956**;66:259–265
27. Sarwar M, Crelin ES, Kier EL, Virapongse C. Experimental cord stretchability and the tethered cord syndrome. *AJNR* **1983**;4:641–643
28. Streeter GL. Factors involved in the formation of the filum terminale. *Am J Anat* **1919**;25:1–11
29. Mapstone TB, White RJ, Takaoka Y. Anterior sacral meningocele. *Surg Neurol* **1981**;16:44–47
30. Goldstein F, Kepes J. The role of traction in the development of the Arnold-Chiari malformation. An experimental study. *J Neuropathol Exp Neurol* **1966**;25:654–666
31. Gryspeerdt GL. Myelographic assessment of occult form of spinal dysraphism. *Acta Radiol [Diagn]* (Stockh) **1963**;1:702–717
32. Naidich TP, McLone DG, Mutluer S. A new understanding of dorsal dysraphism with lipoma (lipomyeloschisis): radiologic evaluation and surgical correction. *AJNR* **1983**;4:103–116, *AJR* **1983**;140:1065–1078
33. Emery JL, Naik DR. Spinal cord segment lengths in children with meningomyelocele and the Cleland-Arnold-Chiari malformation. *Br J Radiol* **1968**;41:287–290
34. Naik DR, Emery JL. The position of the spinal cord segments related to the vertebral bodies in children with meningomyelocele and hydrocephalus. *Dev Med Child Neurol [Suppl]* **1968**;16:62–68
35. Yamada S, Zinke DE, Sanders D. Pathophysiology of "tethered cord syndrome." *J Neurosurg* **1981**;54:494–503
36. Naidich TP, Harwood-Nash DC. Diastematomyelia: hemicord and meningeal sheaths; single and double arachnoid and dural tubes. *AJNR* **1983**;4:633–636
37. James CCM, Lassman LP. Diastematomyelia. *Arch Dis Child* **1958**;33:526–539
38. James CCM, Lassman LP. Diastematomyelia: a critical review of 24 cases submitted to laminectomy. *Arch Dis Child* **1964**;39:125–140
39. James CCM, Lassman LP. Diastematomyelia and the tight filum terminale. *J Neurol Sci* **1970**;10:193–196
40. Gardner WJ. Hydrodynamic mechanism of syringomyelia: its relationship to myelocele. *J Neurol Neurosurg Psychiatry* **1965**;28:247–259
41. Gardner WJ. Klippel-Feil syndrome, iniencephalus, anencephalus, hindbrain hernia and mirror movements. *Childs Brain* **1979**;5:361–379
42. Warkany J, Wilson JG, Geiger JF. Myeloschisis and myelomeningocele produced experimentally in the rat. *J Comp Neurol* **1958**;109:35–65
43. Brierley JB, Field EJ. The connections of the spinal subarachnoid space with the lymphatic system. *J Anat* **1948**;82:153–166
44. Coben LA, Smith KR. Iodide transfer at four cerebrospinal fluid sites in the dog: evidence for spinal iodide carrier transport. *Exp Neurol* **1969**;23:76–90
45. Hammerstad JP, Lorenzo AV, Cutler RWP. Iodide transport from the spinal subarachnoid fluid in the cat. *Am J Physiol* **1969**;216:353–358
46. Lorenzo AV, Hammerstad JP, Cutler RWP. Cerebrospinal fluid formation and absorption and transport of iodide and sulfate from the spinal subarachnoid space. *J Neurol Sci* **1970**;10:247–258
47. Lichtenstein BW. Spinal dysraphism. Spina bifida and myelodysplasia. *Arch Neurol Psychiatr* **1940**;44:792–810
48. Cameron AH. The Arnold-Chiari and other neuro-anatomical malformations associated with spina bifida. *J Pathol* **1957**; 73:195–211
49. Mackenzie NG, Emery JG. Deformities of the cervical cord in children with neurospinal dysraphism. *Dev Med Child Neurol [Suppl]* **1971**;25:58–67