The Syrinx as a Biological Pothole

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Definition and clinical context

- Syringomyelia (Gr. syrinx-pipe and myelos-marrow) denotes a tubular cavity in the spinal cord. It is most commonly associated with an extramedullary lesion at the foramen magnum.
  - 50% of these are Chiari malformations
  - Other associated lesions include the Dandy-Walker malformation, arachnoiditis from trauma or hemorrhage, meningioma, and skeletal abnormalities such as basilar impression
- In these cases the syrinx nearly always involves the cervical cord and extends for a variable distance caudally

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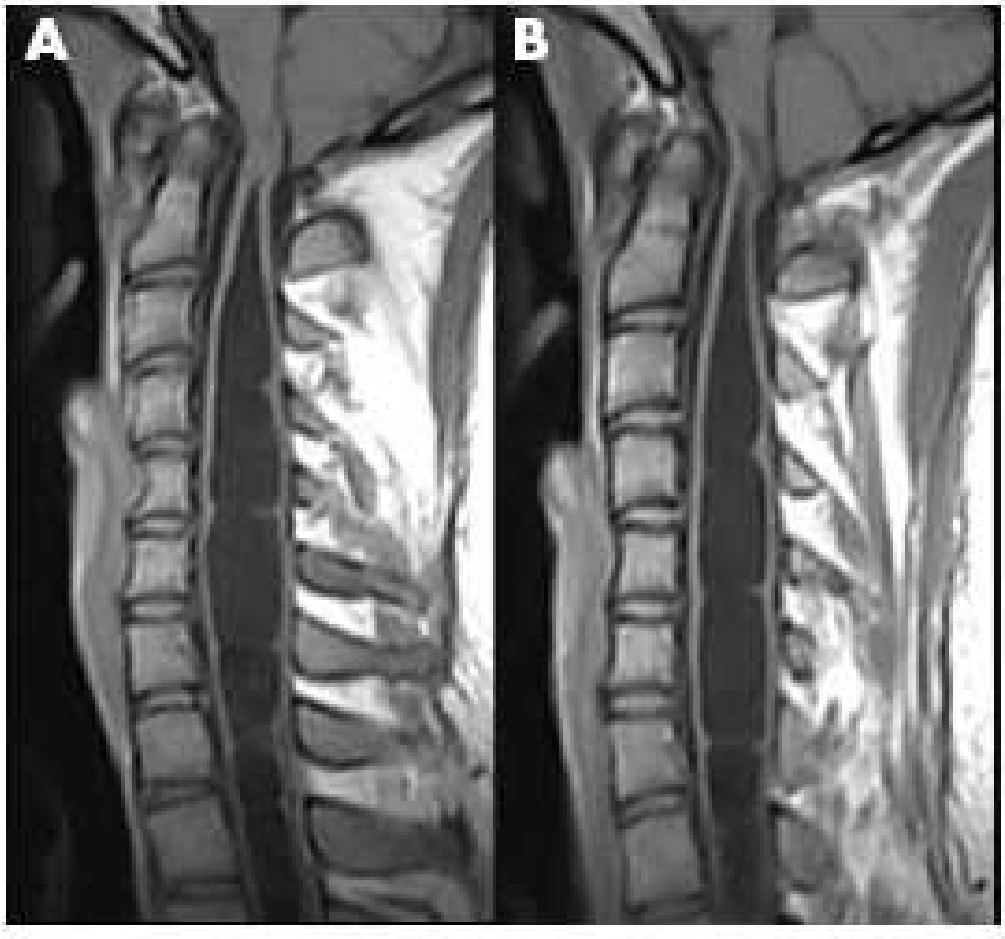
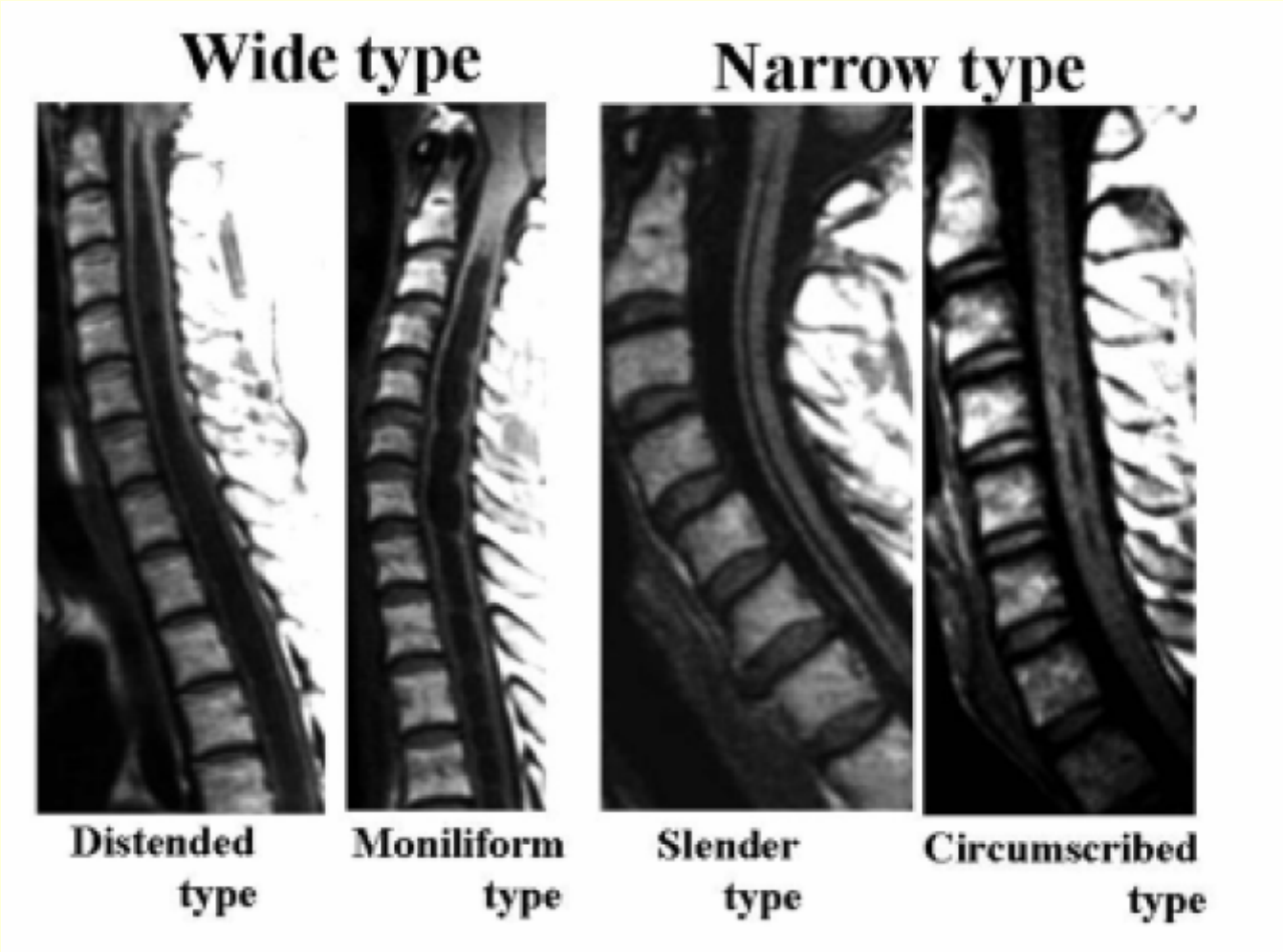


J Neurosurg Spine 6:216,2006



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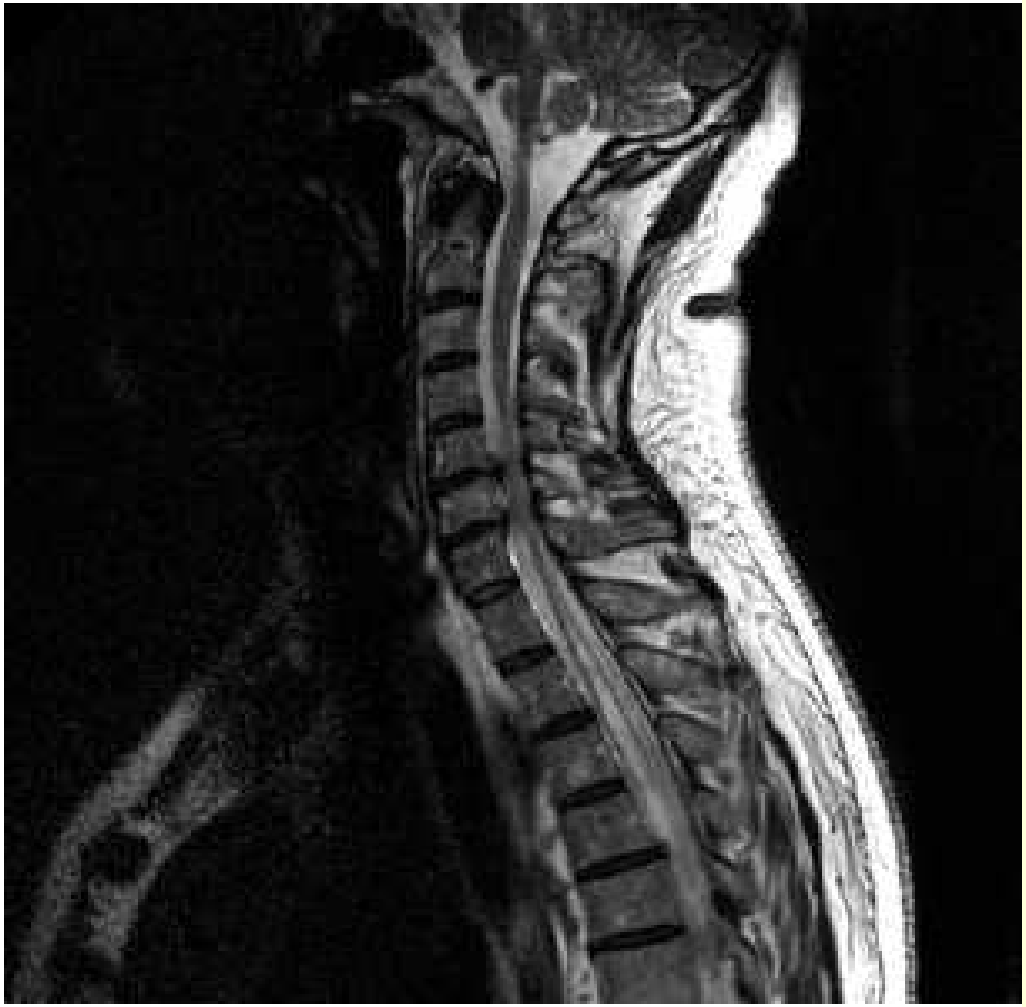


Neuropathology

- Two types of cases
  - Communicating
    - Syrinx is a round or oval ependyma-lined dilation of the central canal that opens into the fourth ventricle
    - Occurs in infants with hydrocephalus and CMII
  - Non-communicating
    - Syrinx is an irregular forked or branching cavity ending rostrally several segments caudal to the fourth ventricle
    - Most commonly occupies gray matter
    - Lined by connective tissue, glia or ependyma in different regions
    - Extensive gliosis surrounds the cavity and also occurs in non-cavitated sheets
    - Abnormal blood vessels with enlarged lumens and thickened walls
    - Occurs most often in adults with CMI

Early theories of pathogenesis

- Controversy was whether SFM was a developmental malformation or an acquired disorder
  - Developmental mechanism was a postulated failure to approximate the lateral plates of the primitive neural tube to obliterate its dorsal portion to form a dorsal medial septum
    - Occurrence of SFM with clearly acquired lesions such as meningioma ruled out the developmental theory
  - Acquired mechanisms were either ischemia or “lymph stasis” of the central cord leading to gliosis with subsequent degeneration and fluid accumulation.
    - Lack of pathological evidence of occlusive vascular disease and infarction and lack of a mechanism for “lymph stasis” rendered the early theories of acquired disorder implausible

Early hydrodynamic theories

- Majority of modern investigators believe that SFM is caused by a disturbance in CSF circulation
  - Gardner: Delay in perforation of the roof of the rhombencehalon lead to failure to dissect open the SA space. Exaggerated pulsations from the ventricle are directed to the central canal causing hydromyelia
  - Williams: FM lesion acts as a valve allowing CSF to pass rostrally more easily than caudally. Activities such as coughing lead to rostro-caudal pressure difference at FM causing fluid from the fourth ventricle to be sucked into the central canal of the spinal cord
- Gardner's theory does not explain why only a minority of patients with SFM have hydrocephalus. Neither theory can explain non-communication syringomyelia, the most common form.

Modern hydrodynamic theories

- The source of syrinx fluid is not CSF from the fourth ventricle but rather CSF from the spinal subarachnoid space
  - Ball & Dayan – Coughing or straining increases epidural venous pressure and therefore CSF pressure. CSF cannot move intracranially and is diverted into the spinal cord along the Virchow-Robin spaces
  - Aboulker – CSF produced in the spinal compartment is normally drained rostrally. In the presence of an FM lesion there is excessive entry of CSF into the cord
  - Oldfield, Heiss, Levy – Cardiac pulsations in the spinal SA space are exaggerated by the “piston” effect of the cerebellar tonsils obstructing the FM driving CSF into the cord along the perivascular spaces

Biophysical critique

- Mean pressure of syrinx fluid greater than that of CSF in SA space – a problem for every theory postulating net flow of CSF from SA space into syrinx.
- Piston mechanism of cerebellar tonsil is questionable, since cerebellar excursions merely replace those of CSF in accommodating intracranial systolic increase in blood volume – problem for Oldfield theory
- Increase in pressure of epidural veins should be transmitted immediately to veins of spinal cord which should expand and increase interstitial fluid pressure – problem for Ball and Dayan theory
- Complete FM block leads to lower CSF pressure in the spinal than in the cranial SA space. If drainage were normally rostral, the spinal SA pressure should rise above the cranial SA pressure as undrained fluid builds up – problem for Aboulker theory
- It is questionable whether a CSF circulation through perivascular spaces of the cord actually exists, and if it does, the changes in CSF pressure in the SA space do not constitute an adequate pump, as the same pressure is being applied to the periarteriolar space input as to the perivenular space output

Other problems with current hydrodynamic theories

- No hydrodynamic theory explains:
  - Dilated and thick walled vessels within and around syrinx cavities. If fluid were being forced in along perivascular channels, veins and capillaries should collapse
  - Widespread gliosis which is often solid and without cavitation
  - Differences of chemical composition – e.g. protein content – of syrinx fluid and CSF

A new theory:
I. Cranial-spinal pressure difference

- The lesion at the foramen magnum acts as a one–way valve and creates repetitive transient episodes of cranial-spinal CSF pressure differences due to:
  - CSF pressure pulsations during the cardiac cycle
  - Coughing
  - Release of Valsalva in straining
  - Assuming the erect posture
- In contrast the venous blood column is unbroken and venous blood pressure remains continuous throughout the craniospinal column

A new theory:
II. Stress from uneven expansion

- Transmural venous pressure decreases above the block, causing capillary and venous collapse
- Transmural venous pressure increases below the block causing capillary and venous expansion
- In the areas just below the block and just above it there is a non-linear, step-like change in tissue volume which creates stresses in the tissue of the spinal cord
  - Such stress is directly analogous to thermal stress in materials that results from uneven volume change due to non-uniform heating

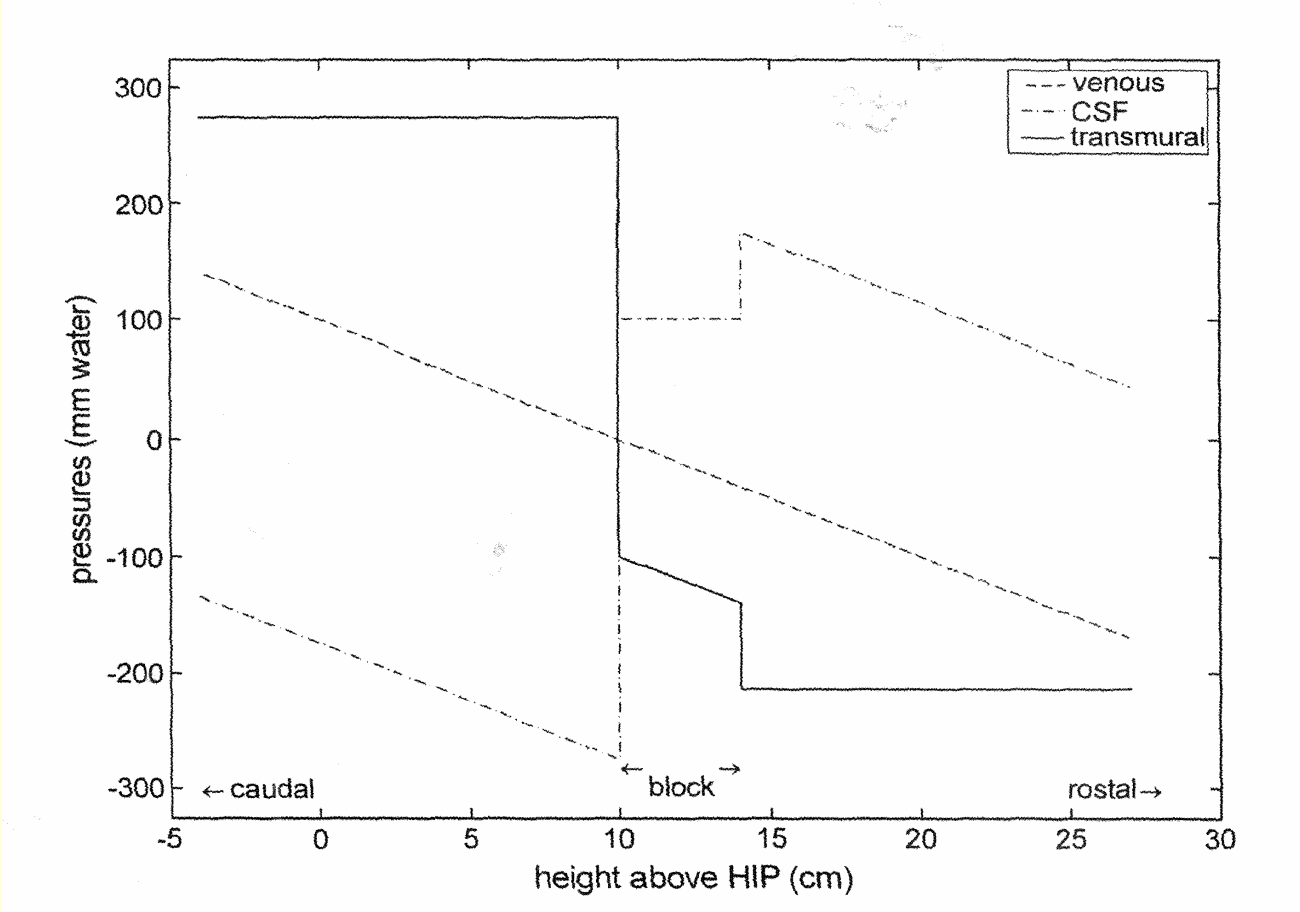
A new theory:
III. Gliosis and plasma ultrafiltration

- Repeated tissue stress causes tissue damage where the stresses are greatest
  - Damage consists of disruption of neuropil, demyelination, and tearing of axonal and cell membranes
  - Tissue damage stimulates chronic gliosis
  - Tissue damage also disrupts the blood brain barrier, particularly below the block where capillaries and veins are distended.
    - Tight junctions between capillary endothelial cells loosen
    - Crystalloids leak producing edema of the cord that is an ultrafiltrate of plasma.
    - Fluid may drain into open segments of the central cord, causing it to distend

Modeling the effects of stress from non-uniform expansion

- Consider the spinal cord to be a circular cylinder that is homogeneous and isotropic
- Assuming the upright posture in the presence of a rigid FM block creates two distinct hydrostatic CSF columns, one above the block and the other below it
- The column of venous blood remains continuous

CSF, venous and transmural pressures



Equations

- The equations of thermal stress for a circular cylinder with circularly symmetric stresses and surface forces are:

$$(\lambda + G)\frac{\partial e}{\partial r} + G\nabla^2 u - \frac{E}{1-2\nu}\frac{\partial(\alpha T)}{\partial r} = 0$$

$$(\lambda + G)\frac{\partial e}{\partial z} + G\nabla^2 w - \frac{E}{1-2\nu}\frac{\partial(\alpha T)}{\partial z} = 0$$

- r & z are radial & axial coordinates; u & w are radial & axial displacements; e is volumetric strain; E is Young's modulus; ν is the Poisson ratio; $G = \frac{E}{2(1+\nu)}$ $\lambda = \frac{\nu E}{(1+\nu)(1-2\nu)}$

Boundary conditions

- Surface of cylinder free of external stress
  - On the curved surface

$$\sigma_r = 0 = \lambda e + 2G\frac{\partial u}{\partial r} - \frac{E\alpha T}{1-2\nu}$$

$$\tau_{rz} = 0 = \frac{\partial u}{\partial z} + \frac{\partial w}{\partial r}$$

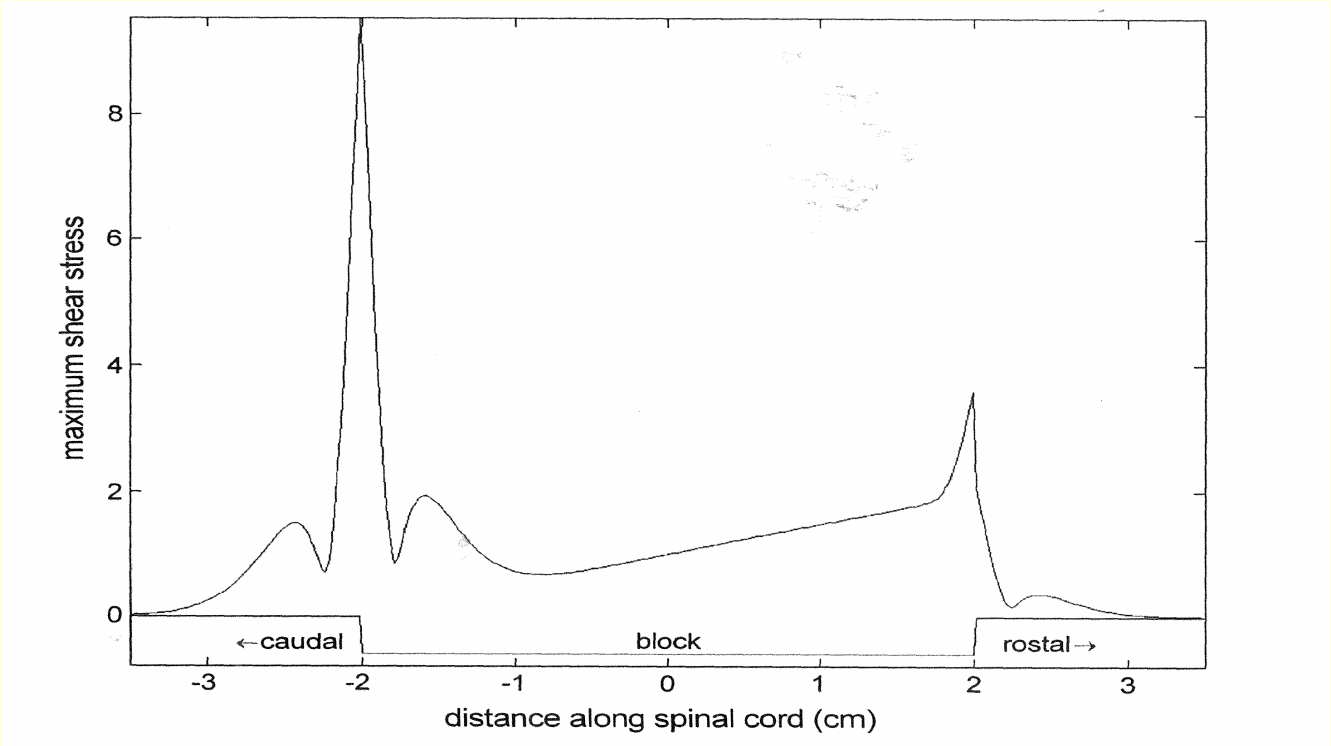
  - On the cross-sections at the two ends

$$\sigma_z = 0 = \lambda e + 2G\frac{\partial w}{\partial z} - \frac{E\alpha T}{1-2\nu}$$

$$\tau_{rz} = 0 = \frac{\partial u}{\partial z} + \frac{\partial w}{\partial r}$$

Solution

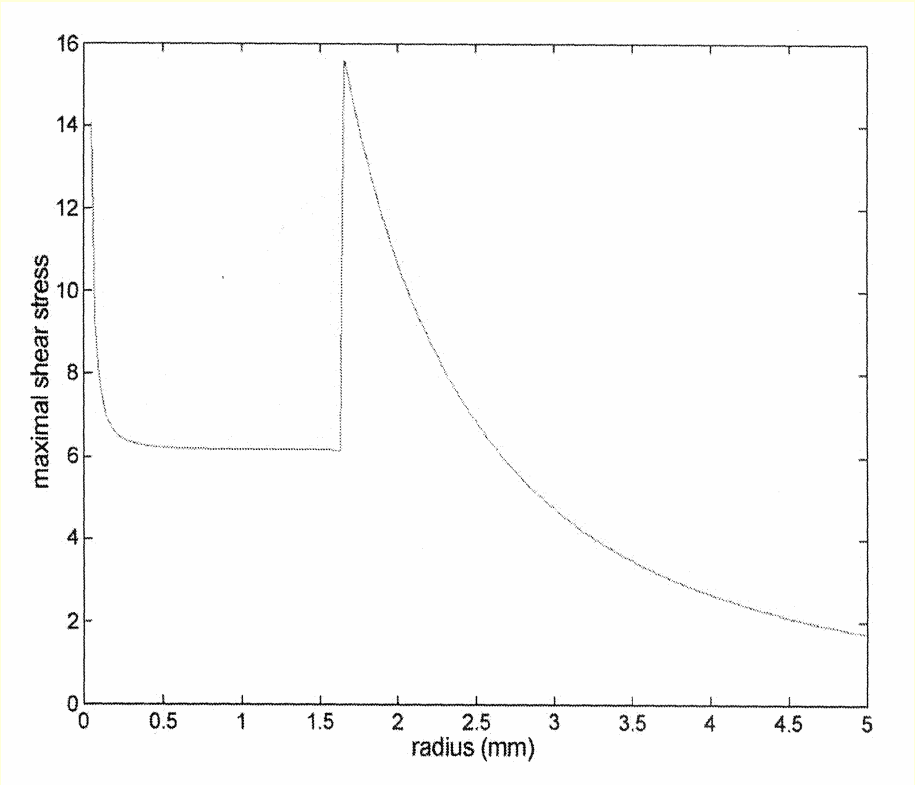
- Equations were solved by a method suggested by Timoshenko and Goodier with the help of a finite–element method implemented in MATLAB



Axial stress distribution

- One can calculate the stress distribution in an axial cross section caudal to the block with the aid of a slightly more complex model of a circular cylinder with a central hole (central canal) and concentric central gray matter surrounded by an annulus of peripheral white matter.
- The same equations can be solved analytically

Axial stress distribution



- Radii:
  - Spinal cord: 5 mm
  - Central gray: 1.7 mm
  - Central canal: 0.05 mm

Prediction of syrinx location - I

- The first model shows that with assumption of the upright posture stress concentrates at the caudal and at the cranial borders of the block
  - The caudal border is the more likely site of syrinx formation, as the vessels dilate only caudal to the block
  - Although not modeled, additional longitudinal stress concentration should occur where the ratio of gray to white matter is changing most rapidly – in the regions of the cervical and lumbar enlargements

Prediction of syrinx location - II

- The second model shows that stress concentrates at the central canal and at the gray-white junction
- Stress is higher in gray matter than in white matter and higher centrally than peripherally
- The anterior median sulcus and the dorsal median septum, although not modeled, would be expected to increase stress concentration in the midsagittal plane near the central canal.

Neuropathological predictions

- General topographic features of non-communicating SFM
- Extensive gliosis, even without cavitation, as a reaction to chronic repetitive stress
- Thick-walled dilated vessels, because the stress results from repetitive vasodilation
- Edema as a result of ultrafiltration of plasma from disrupted endothelial tight junctions
- Syrinx pressure will equal or exceed CSF pressure in the SA space
  - Ultrafiltration results in elevation of the interstitial fluid pressure which was initially equal to CSF pressure in the SA space. With increasing damage fluid may collect in the central canal and in foci of disrupted tissue.
  - If the syrinx is isolated from the SA space by fibrosis and gliosis, syrinx pressure will rise further to equal capillary hydrostatic pressure minus capillary oncotic pressure

Temporal course

- Stress from uneven expansion produces cumulative damage over a long time, similar to repetitive low-intensity stress to other tissues. This accounts for the slowly progressive nature of syringomyelia in the majority of patients
- The theory also is consistent with the precipitation or aggravation of symptoms of syringomyelia by straining, severe coughing or sneezing, or by assumption of the erect posture