spinal fluid waves and the pathogenesis of syringomyelia

By Erika Lindgren, Marie Rognes, Kent-Andre Mardal, and others

# Introduction

## The purpose of this paper is to provide background information for studies in Cerebrospinal fluid hydrodynamics and specifically its role in the pathogenesis of syringomyelia. The paper includes descriptions of relevant cranial and spinal anatomy, pathology, spinal fluid flow characteristics, and selected l computational studies on cerebrospinal fluid flow. It hopefully provides a guide for future research in spinal fluid dynamics as a recent review paper does for researchers in brain mechanics.

The purpose of this presentation is to discuss CSF velocity and pressure waves in relationship to the pathogenesis of syringomyelia. Fluctuations in CSF pressure and velocity are familiar to neuroradiologists.

The concept of fluid waves originating in the cranial vault and propogating down the cervical spine is less familiar. This discussion requires expertise in fluid dynamics , such as my co-presenter Erika has. Waves have many interesting dynamics, which may have relevance to the pathogenesis of syringomyelia. Changes in the wave as it passes downward along the spinal canal may result in a shock wave, or another feature that may critically affect the spinal cord. Introduce EL, an expert on fluid dynamics who will describe features of flow and waves in closed channels

## Definition and Description of Syringomyelia

# The medical term “Syringomyelia” applies to fluid-containing cysts within the spinal cord. While Syringomyelia may be differentiated from “Hydromyelia ” by microscopic examination of the spinal cord the two terms are often used interchangeably or replaced by the term “Syringo-hydromyelia” when the microscopic anatomy is not available. By microscopy, two cyst types are recognized: cystic dilatation of the central canal in the spinal cord (hydromyelia) and a cyst formation in the spinal cord parenchyma outside the central canal (syringomyelia). Ependymal cells, which form the lining of the central canal in the spinal cord, surround cysts that are classified as hydromyelia while glial cells, that populate the spinal cord tissue, surround cysts that are classified at syringomyelia. Both may occur simultaneously. Hydromyelia may convert to syringomyelia if the cyst in the central canal ruptures into the cord parenchyma.

# Syringomyelia occurring without associated trauma, tumor, vascular malformation, infection or other obvious cause is designated Idiopathic Syringomyelia. Cysts in patients with Idiopathic Syringomyelia in theory develop because of abnormal spinal fluid dynamics. Similar cysts occur in 30 to 50% of patients with the Chiari I malformation, which is defined by the presence of cerebellar tonsils extending abnormally into the upper cervical spinal canal. In both Idiopathic Syringomyelia and Chiari I the cysts contain clear fluid, nearly indistinguishable from Cerebrospinal fluid. Syringomyelia occurs also in animals, notably in association with a malformation similar to the Chiari malformation occurs in the King Charles Cavalier Spaniel.

# Syringomyelia presents most commonly in the second decade of life and most commonly in Chiari patients. Syringomyelia develops typically at or below the sixth cervical vertebra, although any spinal level may be affected. Because of the association of syringomyelia with abnormal tonsil position, the cysts are assumed to result from abnormal cerebrospinal fluid dynamics. The treatment for syringomyelia, either idiopathic or associate with the Chiari malformation is craniovertebral decompression, that is surgical enlargement of a portion of the upper spinal canal and of the lower cranial vault. The surgery leads to the resolution of the syrinx in most patients over a period of several weeks to months. The operation assumedly changes fluid dynamics to favor fluid escaping from the cord.

# How the anatomy of the cranium and spine and the physiology of CSF flow result in the syringomyelia remains unclear. While tonsilar position is a factor, it develops uncommonly at the level of the tonsils and usually not at the narrowest portion of the cervical spinal canal, which is C4. Multiple theories have been proposed to explain the pathogenesis of syringomyelia and most have been to some degree been discredited. Research on syringomyelia presently focuses on the fluid dynamics in the subarachnoid space and its effect on the spinal cord.

The Cerebrospinal fluid has an oscillatory flow pattern due to the expansion of the brain with each cardiac systole increases pressure in the cranial vault normally by about 4 cm water. Because of the limited compliance of the cranial vault and the incompressibility of cerebrospinal fluid and brain tissue, some Cerebrospinal fluid is forced out of the cranial vault into the spinal canal (about 1 – 2 mL for each heart beat). This pressure wave that moves through the cranial and spinal subarachnoid space. The spinal subarachnoid space, having about twice the compliance of the cranial vault (Alperin), accommodates the fluid expelled from the cranial vault and returns it to the cranium during diastole. In patients, with syringomyelia, CSF flow in and out of the cranial vault is hyperactive, because the compliance of the cranial vault is decreased in these patients .

# Anatomy of the Subarachnoid Space

## Cranial

The subarachnoid space encloses the Cerebrospinal fluid, cerebrum, cerebellum, brain stem and spinal cord. The Cerebrospinal fluid has an oscillatory flow pattern due to the expansion of the brain with each cardiac systole that increases pressure in the cranial vault, normally by about 4 cm water (Alperin). It produces a pressure wave that moves through the subarachnoid space at 2 to 4 m/sec (reference). Because of the limited compliance of the cranial vault and the incompressibility of cerebrospinal fluid and brain tissue, some Cerebrospinal fluid is forced out of the cranial vault into the spinal canal (about 1 – 2 mL for each heart beat)(reference: ). The spinal subarachnoid space, having about twice the compliance of the cranial vault (Alperin), accommodates the fluid expelled from the cranial vault and returns it to the cranium during diastole. CSF has higher velocities in the caudal direction and slower velocities in the cranial direction. In some patients, notably patents with the Chiari malformation, CSF flow in and out of the cranial vault is hyperactive, because the compliance of the cranial vault is decreased in these patients. CSF velocities increase from C1 to C4 in normal individuals and in Chiari I patients, due to the tapering of the spinal canal (Shah).It has normally a linear velocity at the foramen magnum of 2 to5 cm/sec. Patients with Chiari I or Idiopathic Syringomyelia have more complex CSF dynamics and greater velocities than normal individuals (Quigley). They have more conspicuous synchronous bidirectional flow and flow jets. They may have less stable flow patterns (Helgeland).

## Posterior Fossa

The Posterior Fossa, divided from the cranial vault by a stiff membraned, the Tentorium, houses the cerebellum and brain stem that connects the brain with the spinal canal as the spinal cord. The cerebellum has a pair of tissue extension, the cerebellar tonsils, which are normally contained within the posterior fossa. In patients with the Chiari I malformation the tonsils extend into the spinal canal. Extension of the tonsils 5 mm into the canal is accepted as the definition of the malformation since a seminal study (Barkovitch) demonstrated most symptomatic Chiari I patients had greater than 5 mm of herniation. However, patients with less extension or no extension may be symptomatic (Medows). Posterior fossa dimensions show are smaller in patients with the Chiari I malformation (Spiros). To measure the volume of the complex shape of the posterior fossa, investigators measure lengths of specific structures and linear dimensions related to it. These measurements show smaller volumes of the posterior fossa in patients with the Chiari I malformation, suggesting that the tonsilar extension may be secondary to the diminutive posterior fossa. These studies have not distinguished between Chiari patients with and Chiari patients without syringomyelia. Measurements in patients with Idiopathic Syringomyelia (Bogdanov) show that the posterior fossa is smaller than normal in these patients also. Investigators, who have measured the compliance of the cranium and posterior fossa, findita decreased in patients with the Chiari malformation. Whether the abnormal compliance is due to the smaller dimensions, the position of the tonsils, or another abnormality such as pathologic venous anatomy or function is not known.

*The Posterior fossa dimensions are smaller in patients with Idiopathic Syringomyelia or syringomyelia with Chiari I malformation (Spiros). This may explain diminished compliance. This means a greater change in pressure for a specific change in volume in the cranial vault or in other word a wave of greater amplitude,*

## Cervical Spine

Cervical spinal anatomy and specifically the shape and size of the subarachnoid space hypothetically affect the oscillatory flow of cerebrospinal fluid. The spinal canal in normal healthy adults tapers from the Foramen Magnum to C4 and remains roughly constant in diameter below C4 (Tatarek, Hirano, Hammersley). This tapering causes Cerebrospinal fluid velocities to increase from C1 to C4 (Shah). In Idiopathic Syringomyelia, the cervical spinal canal tapers rom Foramen Magnum to C4 and then expands from C4 to C7. Cerebrospinal fluids velocities below C4 have not been have not been adequately characterized in these patients or in normals. In Chiari I patients, Cerebrospinal fluid velocities increase from C1 to C4 (Shah). This pattern of tapering and reverse tapering also characterizes Chiari I patients with syringomyelia, but not those with Chiari I malformation who lack syringomyelia. How the cervical spinal anatomical differences affect cyclic Cerebrospinal fluid flow has not been adequately studied.

## Spinal Cord

The spinal cord contains multiple anatomic features and multiple types of tissue. Gray matter, which has the cell bodies of spinal cord neurons occupies the central part of the spinal cord. It permits interstitial flow without greatly limiting the direction of flow in any direction. The tissue surrounding the gray matter is white matter, which consists of neuronal fiber tracts. These facilitate the movement of interstitial fluid along the long axis of the cord and limits flow transverse to the long axis (Stoverud). The spinal cord has a superficial membrane, the pia mater, which covers the exterior of the cord and may affect the movement of fluid in the spinal cord (Stoverud). A conspicuous feature of the spinal cord is the anterior median fissure, a cleft in the anterior cord, filled with CSF, which extends into the spinal cord all the way to the deep gray matter. This structure brings the cerebrospinal flid pressure wave close to the center of the cord. Another anatomic feature of the spinal cord is a small canal lined with ependymal cells in the gray matter near the center of the cord. This canal, whose function is not well known, is present a birth. Its ependymal cells may facilitate the movement of fluid in or out of the canal. As a person ages, the central canal within the spinal cord develops multiple obstruction (Milhorat), which may restrict flow along the central canal or may hypothetically permit flow only in one direction, due to a ball valve type mechanisms. In adults, much of the central can is obliterated. The presence of the central canal within the cord affects the cord pressures that result from the passage of the cerebrospinal fluid pressure wave through the subarachnoid space (Kylstad thesis). As a result of the central canal pressure changes in the cerebrospinal fluid result in centripetal and centrifugal pressure gradients in the cord. When the central canal is mostly obliterated, as it is in individuals more than 40 years of age, radially directed pressure gradients do not occur in the cord. When it is completely patent, the central canal may facilitate fluid movement longitudinally in the spinal cord because of potential connections to the subarachnoid space via the fourth ventricle and terminus of the cord. Therefore syringomyelia and hydromyelia present when typically isolated segments of the central canal are present.

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Review of imaging and Hydrodynamics:

Haughton V, Mardal K-A. Spinal fluid biomechanics and imaging: an update for neuroradiologists. AJNR Am J Neuroradiol. 2014; 35:1864-9.

Paper by influential neurosurgeon. Interesting to consider partial obstruction of the central canal as a factor in the theory in this paper:

Heiss JD1, Patronas N, DeVroom HL, Shawker T, Ennis R, Kammerer W, Eidsath A, Talbot T, Morris J, Eskioglu E, Oldfield EH. Elucidating the pathophysiology of syringomyelia J Neurosurg. 1999; 91:553-62.

Critique of theories on pathogenesis of syringomyelia, by a relatively obscure writer:

Levine DN. The pathogenesis of syringomyelia associated with lesions at the foramen magnum: a critical review of existing theories and proposal of a new hypothesis. J Neurol Sci. 2004 May 15;220:3-21.

Abstract

Syringomyelia is frequently accompanied by an extramedullary lesion at the foramen magnum, particularly a Chiari I malformation. Although syringomyelia associated with foramen magnum obstruction has characteristic clinical, radiological, and neuropathological features, its pathogenesis remains unclear. Currently prevalent hydrodynamical theories assert that obstruction of the subarachnoid space at the foramen magnum interferes with flow of cerebrospinal fluid (CSF) between the spinal and the intracranial subarachnoid compartments. As a result, spinal CSF is driven into the spinal cord through the perivascular spaces to form a syrinx. These theories are implausible biophysically because none postulates a pump adequate to drive fluid through these spaces. None of the theories can explain why syrinx pressure is higher than CSF pressure; why extensive gliosis, edema, and vascular wall thickening regularly occur ; and why the composition of syrinx fluid is not identical with that of CSF. A new theory of pathogenesis is proposed to address these difficulties. In the presence of subarachnoid obstruction at the foramen magnum, a variety of activities, such as assuming the erect posture, coughing or straining, and pulsatile fluctuations of CSF pressure during the cardiac cycle, produce transiently higher CSF pressure above the block than below it. There are corresponding changes in transmural venous and capillary pressure favoring dilation of vessels below the block and collapse of vessels above the block. The spatially uneven change of vessel caliber produces mechanical stress on the spinal cord, particularly caudal to the block. The mechanical stress, coupled with venous and capillary dilation, partially disrupt the blood-spinal cord barrier, allowing ultrafiltration of crystalloids and accumulation of a protein-poor fluid . The proposed theory is consistent with the neuropathological findings in syringomyelia and with the pressure and composition of syrinx fluid. It also accounts for the prolonged course of syringomyelia and its aggravation by cough, strain, and assumption of an erect posture . It contributes to understanding the low incidence and the morphology of syringobulbia. It explains the poorly understood presentation of foramen magnum meningiomas with symptoms of a mid- to low-cervical myelopathy. The theory also affords an understanding of the late recurrence of symptoms in children with hydromyelia who are treated with a ventricular shunt.

Review of studies using engineering analysis, by the Frank Loth group:

Shaffer N, Martin B Loth F. Cerebrospinal Fluid Hydrodynamics in type I Chiari Malformation. Neurol Res 2011; 33:247 – 60

Review and another hypothesis, from relatively obscure writers:

Koyanagi I, Houkin K. Pathogenesis of Syringomyelia associated with Chiari type I malformation: review of evidence and proposal of a new hypothesis. Neurosurg Rev 2010; 33: 271-84

Well publicized theory, shown by simulations to have invalid assumption that Bernoulli law applies:

Greitz D. Unraveling the riddle of syringomyelia. Neurosurg Rev. Oct 2006; 29:251-63; discussion p. 264.

Abstract

The pathophysiology of syringomyelia development is not fully understood. Current prevailing theories suggest that increased pulse pressure in the subarachnoid space forces cerebrospinal fluid (CSF) through the spinal cord into the syrinx. It is generally accepted that the syrinx consists of CSF. The here-proposed intramedullary pulse pressure theory instead suggests that syringomyelia is caused by increased pulse pressure in the spinal cord and that the syrinx consists of extracellular fluid. A new principle is introduced implying that the distending force in the production of syringomyelia is a relative increase in pulse pressure in the spinal cord compared to that in the nearby subarachnoid space. The formation of a syrinx then occurs by the accumulation of extracellular fluid in the distended cord. A previously unrecognized mechanism for syrinx formation, the Bernoulli theorem, is also described. The Bernoulli theorem or the Venturi effect states that the regional increase in fluid velocity in a narrowed flow channel decreases fluid pressure. In Chiari I malformations, the systolic CSF pulse pressure and downward motion of the cerebellar tonsils are significantly increased. This leads to increased spinal CSF velocities and, as a consequence of the Bernoulli theorem, decreased fluid pressure in narrow regions of the spinal CSF pathways. The resulting relatively low CSF pressure in the narrowed CSF pathway causes a suction effect on the spinal cord that distends the cord during each systole. Syringomyelia develops by the accumulation of extracellular fluid in the distended cord. In posttraumatic syringomyelia, the downwards directed systolic CSF pulse pressure is transmitted and reflected into the spinal cord below and above the traumatic subarachnoid blockage, respectively. The ensuing increase in intramedullary pulse pressure distends the spinal cord and causes syringomyelia on both sides of the blockage. The here-proposed concept has the potential to unravel the riddle of syringomyelia and affords explanations to previously unanswered clinical and theoretical problems with syringomyelia. It also explains why syringomyelia associated with Chiari I malformations may develop in any part of the spinal cord including the medullary conus. Syringomyelia thus preferentially develops where the systolic CSF flow causes a suction effect on the spinal cord, i.e., at or immediately caudal to physiological or pathological encroachments of the spinal subarachnoid space.

Example of a study from the Stoodley group:

Clarke EC, Fletcher DF, Stoodley MA, Bilston LE. Computational fluid dynamics modelling of cerebrospinal fluid pressure in Chiari malformation and syringomyelia. J Biomech. 2013 26;46(11):1801-9.

Abstract

The pathogenesis of syringomyelia in association with Chiari malformation (CM) is unclear. Studies of patients with CM have shown alterations in the CSF velocity profile and these could contribute to syrinx development or enlargement. Few studies have considered the fluid mechanics of CM patients with and without syringomyelia separately. Three subject-specific CFD models were developed for a normal participant, a CM patient with syringomyelia and a CM patient without syringomyelia. Model geometries, CSF flow rate data and CSF velocity validation data were collected from MRI scans of the 3 subjects. The predicted peak CSF pressure was compared for the 3 models. An extension of the study performed geometry and flow substitution to investigate the relative effects of anatomy and CSF flow profile on resulting spinal CSF pressure. Based on 50 monitoring locations for each of the models, the CM models had significantly higher magnitude (p<0.01) peak CSF pressure compared with normal. When using the same CSF input flow waveform, changing the upper spinal geometry changed the magnitude of the CSF pressure gradient, and when using the same upper spinal geometry, changing the input flow waveform changed the timing of the peak pressure. This study may assist in understanding syringomyelia mechanisms and relative effects of CSF velocity profile and spinal geometry on CSF pressure.

Example of a clinical study with MR Measurements:

Pinna G, Alessandrini F, Alfieri A, Rossi M, Bricolo A. Cerebrospinal fluid flow dynamics study in Chiari I malformation: IImplicatiions for syrinx formation. Neurosurg Focus 2000 15:8:E3

Quigley, MF, Iskandar B, Quigley ME, Nicosia M, Haughton V. Cerebrospinal fluid flow in foramen magnum: temporal and spatial patterns at MR imaging in volunteers and in patients with Chiari I malformation. Radiology 2004; 232: 229-236. .

Examples of Papers with Simulations:

Drøsdal IN, Mardal K-A, Støverud K, Haughton V. Effect of the Central Canal in the Spinal Cord on Fluid Movement within the Cord. Neuroradiology Journal 2013; 3: 585-590

Helgeland A, Mardal KA, Haughton V, Reif BA. Numerical simulations of the pulsating flow of cerebrospinal fluid flow in the cervical spinal canal of a Chiari patient. J Biomech 2014; Jan 22. pii: S0021-9290(14)00002-5.

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Rutkowska G, Haughton V, Linge S, Mardal KA. Patient-Specific 3D Simulation of Cyclic CSF Flow at the Craniocervical Region. AJNR Am. J. Neuroradiol 2010; 31:997-1002.

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Loth group:

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Bilston LE, Fletcher DF, Brodbelt AR, Stoodley MA. Arterial pulsation-driven cerebrospinal fluid flow in the perivascular space: a computational model. Comput Methods Biomech Biomed Engin. 2003; 6:235-41

Miscellaneous:

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