The estimated prevalence of syringomyelia in the general population is 1.94 to 8.4 per 100,000 people. The pathogenesis of the formation of a spinal cord syrinx has been debated for some time, with theories originally describing disorderly embryonic cellular development and migration. Recently, the pathophysiology of a syrinx has been believed to originate from disorderly CSF flow. The population of patients with open spinal neural tube defects (NTDs) has long been known to have a much higher rate of syrinx formation (previously cited as 42%–77%) than the general population. The estimated prevalence of syringomyelia in the general population is 1.94 to 8.4 per 100,000 people. The pathogenesis of the formation of a spinal cord syrinx has been debated for some time, with theories originally describing disorderly embryonic cellular development and migration. Recently, the pathophysiology of a syrinx has been believed to originate from disorderly CSF flow. The population of patients with open spinal neural tube defects (NTDs) has long been known to have a much higher rate of syrinx formation (previously cited as 42%–77%) than the general population.

**Object.** Syringomyelia can be diagnosed in isolation but is more commonly found in the presence of cranio-cervical junction anomalies or spinal dysraphism. The origin of syringomyelia has been hypothesized to be either congenital or acquired. The purpose of this study was to determine the incidence of syringomyelia within the fetal and postnatal population with neural tube defects (NTDs).

**Methods.** A review was performed of the authors’ fetal MRI database of pregnancies with imaging between March 2004 and November 2011 for evaluation of an intrauterine anomaly detected via prenatal ultrasonography. Those cases with an NTD were then selected and a chart review was performed of all prenatal and postnatal imaging as well as available clinical history.

**Results.** A total of 2362 fetal MRI examinations were performed, and 109 of these were patients with an NTD. Of the 2362 studies reviewed, 2 cases of fetal syringomyelia were identified. Both fetal syrinxes were identified in fetuses with CSF flow disturbances (1 case each of encephalocele and myelomeningocele). Both fetal MRI examinations were performed late in gestation, at 31 and 38 weeks, respectively. The patient with an encephalocele was excluded from the spinal NTD population; therefore a syrinx was identified in 0.08% (2/2362) of the entire population of fetuses who underwent MRI, or 0.9% (1/109) of fetuses with a spinal NTD. Sixty-three of the 109 patients with an NTD had postnatal clinical data available for review. Twenty-nine (46%) of 63 had a syrinx identified during the follow-up period. Of this group, 50 patients had an open NTD and 27 (54%) of 50 developed a syrinx. Among the patients with an open NTD who developed a syrinx, only 7% did not have or develop hydrocephalus, compared with 35% of the patients who did not develop a syrinx (p < 0.05). There were nonsignificantly more frequent shunt revisions among those patients who developed a syrinx, and a syrinx developed in all patients who required surgical Chiari malformation decompression or tethered cord release. The initial identification of a spinal cord syrinx varied greatly between patients, ranging from 38 weeks gestation to greater than 4 years of age.

**Conclusions.** These data suggest that syringomyelia is not a congenital embryonic condition. A syrinx was not identified in fetuses who underwent imaging for other intrauterine anomalies. In the population of patients with NTDs who are known to be at high risk for developing syringomyelia, the pathology was only identified in 2 third-trimester fetuses or postnatally, typically in the presence of hydrocephalus, shunt placement, Chiari malformation decompression, or tethered cord release. The study supports the authors’ hypothesis that a syrinx is an acquired lesion, most likely due to the effects of abnormal CSF flow.
Pre- and postnatal evaluation for a syrinx in spinal dysraphism

The increased incidence of syringomyelia among these patients has been variously attributed to abnormal CSF flow in the intracranial compartment, at the foramen magnum, and at the neural placode. Currently, there are little reported data regarding the timing of syrinx formation relative to embryonic and fetal development. A PubMed literature search using the key words “fetal syringomyelia,” “syringomyelia,” “spinal cord syrinx,” and “fetal MRI” revealed only 2 reported cases of syringomyelia in a fetus; both of these cases were identified using ultrasonography and not the more reliable MRI. Magnetic resonance imaging is being used with increasing frequency in the fetal population for more accurate diagnosis of fetal malformations. The descriptive accuracy of this anatomical imaging modality is far superior to that of fetal ultrasonography.

We conducted an Institutional Review Board–approved retrospective, nonrandomized review of the CCHMC fetal MRI database from March 2004 through November 2011, searching for the terms “syrinx” or “syringomyelia.” A waiver of authorization was obtained from the Institutional Review Board so that consent would not need to be obtained for any patient involved in this retrospective chart review. All fetal MR images were read by a specialized pediatric neuroradiologist and performed between 16 and 38 weeks gestation for the indications of an anomaly detected via prenatal ultrasonography. To identify anatomical fetal anomalies, MRI was performed with a 1.5-T magnet using 3 different types of sequences: T2-weighted single-shot fast spin echo, 2D fast imaging employing steady-state acquisition (FIESTA), and T1-weighted spoiled gradient-recalled acquisition. The imaging diagnostic criteria used for a fetal syrinx were a tubular CSF space in the spinal cord identified on consecutive images and in at least 2 planes.

A second search of the fetal MRI database was then performed, searching for examinations with the radiological diagnosis of NTD. The CCHMC Fetal Care Center serves as a large referral center for the region surrounding Cincinnati, Ohio. All patients (mothers) who were referred to the Fetal Care Center for evaluation underwent fetal MRI for anatomical evaluation of the fetus. However, due to the large referral base of the hospital, there is a minor population of patients with NTDs who were treated at CCHMC who were not examined in the Fetal Care Center, and these patients were not included in any part of the review. The MRI reports containing a diagnosis of fetal NTD were individually reviewed, searching for the presence of a syrinx or ventriculomegaly, identifying the level of dysraphism, and identifying whether the defect was either an open or closed NTD. The CCHMC electronic medical record system was then queried, searching for postnatal follow-up of all patients with an NTD who underwent fetal MRI. The standard protocol within the CCHMC pediatric neurosurgical division is for initial postnatal complete cranial/spinal MRI to be completed before the infant leaves the neonatal intensive care unit if clinically possible, with scheduled repeat imaging obtained at 12 months and 3 years of age, but variation occurs due to clinical symptomatology. These charts were searched for the presence of a postnatal syrinx, the presence or absence of associated ventriculomegaly, and the need for surgical procedures including CSF diversion, surgical revision of CSF shunt devices, surgical decompression of a Chiari malformation, and tethered cord release.

Data were analyzed using nonparametric statistics. We used the Fisher’s exact and chi-square tests for categorical variables. Statistical calculations were performed with PASW statistics gradpack (version 20.0, SPSS Inc.). Statistical significance was set at p < 0.05.
completely random and should not instill any selection bias. Fifty of these 63 patients had open NTDs and 13 of these 63 patients had closed NTDs (meningocele, lipomyelomeningocele, and terminal myelocystocele). The rate of postnatal syrinx formation in the open NTD population was 54% (27/50; Table 1, Fig. 2). Among the open NTD population there was only 1 patient who received their initial postnatal MRI prior to closure of the NTD. Four of the patients with open NTDs underwent intrauterine repair of their NTD and all other patients received their initial imaging following surgical closure of their NTD. The rate of postnatal syrinx formation in the closed NTD population was 15% (2/13; Table 1). Within the subset of patients with an open NTD, there was a significant difference (p < 0.05) in the number of patients who did not require a shunt for hydrocephalus among the group of patients who developed a syrinx (7%) compared with those who did not develop a syrinx (35%; Table 2). There were more surgical shunt revisions among the group that developed a syrinx compared with those who did not develop a syrinx, but this difference did not reach statistical significance (0.73). There was a significantly greater number of Chiari malformation decompressions (30% vs 0%, respectively; p = 0.004) and nonsignificantly more frequent tethered cord release operations (11% vs 0%, respectively; p = 0.236) in the patients with an open NTD who developed a syrinx compared with those who did not develop a syrinx.

Finally, the time to develop a syrinx varied widely within the group of patients with open NTDs, ranging from 38 weeks’ gestation to greater than 4 years of life (Fig. 3). However, excluding the patient with an encephalocele, no patient developed a syrinx prior to 38 weeks gestational age, and only 1 (1.1%) had a syrinx detected on prenatal imaging, which contrasts starkly with the

<table>
<thead>
<tr>
<th>NTD</th>
<th>Prenatal Syrinx</th>
<th>Postnatal Syrinx</th>
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<tbody>
<tr>
<td>open</td>
<td>1.1% (1/91)</td>
<td>54% (27/50)</td>
</tr>
<tr>
<td>closed</td>
<td>0% (0/18)</td>
<td>15% (2/13)</td>
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The pathophysiology of syringomyelia continues to not be entirely understood. The original embryonic theories of the late 1800s and early 1900s described histopathological features of failed neural tube closure and subsequent dilution of the abnormally formed lumen of the tube. These descriptions were soon replaced by the more commonly accepted theories such as the Gardner “water hammer theory,” which postulated that a syrinx developed secondary to CSF pulsations through the obex into the central canal. This theory was altered by Williams when he described CSF flowing from the spinal cistern through the foramen magnum during elevations in intrathoracic pressure, and then becoming trapped due to obstruction at the foramen magnum, leading to flow through the obex into the central canal. More recent descriptions have postulated that CSF enters the central canal through the Virchow-Robin perivascular spaces of the spinal cord due to elevated pressure in the spinal subarachnoid space secondary to obstructed CSF flow at the foramen magnum. All of these theories are similar in that they describe a potential space within the central canal of the spinal cord developing due to a CSF pressure differential in the presence of obstruction of normal flow at the foramen magnum. It remains unclear from what site the CSF enters the potential space in the spinal cord to create a syrinx. The other forms of syringomyelia that do not relate to obstructed CSF flow in the region of the foramen magnum include traumatic syringomyelia, tumor-associated syringomyelia, syringomyelia secondary to arachnoiditis, and idiopathic syringomyelia.

In our population of fetuses imaged due to a primary obstetrics ultrasonography anomaly, there was an extremely low incidence of a syrinx (0.08%). Therefore, it is postulated that the rate of fetal syringomyelia within the general population would be even lower. Even within the population of patients with an open spinal NTD, we identified a surprisingly low incidence of fetal syringomyelia of 1.1%. This contrasts with the much higher rate of syringomyelia noted in this population postnatally, as high as 54% by the age of 5 years in our own series. Even our single case of fetal syringomyelia in the population of fetuses with open NTDs was identified late in gestation (at 38 weeks). To our knowledge there have been only 2 reported cases of fetal syringomyelia in the literature using fetal ultrasonography, but no reported cases using fetal MRI, which is known to be much more accurate than fetal ultrasonography. These findings would support our theory that a spinal cord syrinx is unlikely to be of embryonic origin and the term “congenital syringomyelia” may be obsolete.

Our rate of syrinx development in the postnatal open NTD population was 54%, which is consistent with percentages previously described in the literature. The higher rate of syrinx development within this population has been attributed to the other associated anomalies observed in these patients including hydrocephalus, hindbrain malformation, and tethered spinal cord. The “unified theory” proposed by McLone and Knepper in 1989 describes...
the NTD as the original inciting factor that results in the
development of the other associated anomalies, including
the Chiari Type II malformation and hydrocephalus. Although fetal imaging did not identify a syrinx in most of
the patients with open NTDs prenatally, a high percentage
developed a syrinx postnatally. In fact, the incidence
of postnatal syringomyelia appeared to increase over the
5-year follow-up period, suggesting that further longitudi-
ental follow-up studies may be helpful to more clearly de-
define the ongoing development of postnatal syringomyelia
over time. In addition, it is interesting that those patients
who had a syrinx underwent more surgical interventions
for hydrocephalus, symptomatic Chiari Type II malfor-
mations, and tethered cord. Our results would support
McLone and Knepper’s theory regarding the relationship
of hydrocephalus and the development of postnatal syr-
ningomyelia within the population of patients with open
NTDs. This could be a subject for further research, as
the reported incidence of downward hindbrain herniation
and hydrocephalus may be decreased in the population
of patients with open NTDs who undergo intrauterine
repair. Our own data on syringomyelia in patients with
intrauterine repair of open NTDs are limited to only 4
patients, so no firm conclusions can be drawn from these
data; however, results of the multicenter randomized trial
of prenatal versus postnatal repair of myelomeningocele
published in 2011 suggest a reduction in the incidence of
syringomyelia from 58% to 39% at 12 months in those
who underwent fetal repair compared with those who did not.

The concept that syringomyelia is acquired in postna-
tal life is further supported by our data on the lower inci-
dence of syringomyelia in patients with closed NTDs. The
rate of postnatally detected syringomyelia in patients with
closed versus open NTDs (15% vs 54%, respectively) can
be explained at least in part by the absence of both hind-
brain herniation and hydrocephalus in most patients with
closed NTDs. All of these findings would support the the-
ory that the syrinx is an acquired, not congenital, anomaly.

The limitations of this study include the lack of late-
gestation fetal MRI in the open NTD population. This
may better define the timing of syrinx development. One
could also question whether early fetal MRI may have
limited detail in defining a fetal syrinx. However, heavily
T2-weighted FIESTA sequences used in the evaluation
of the fetal spine provide excellent detail. Further areas
of deficiency in the study include follow-up of those pa-
tients with a syrinx to determine if surgery for hindbrain
malformation, hydrocephalus, or tethered cord resulted in
resolution of the syringomyelia.

Conclusions

To our knowledge, these are the first reported data on
the incidence of fetal syringomyelia (0.08%) identified us-
ing fetal MRI within a population of patients with prede-
termined congenital anomalies, and the first description
of the incidence of fetal syringomyelia within the popu-
lation of patients with NTD (0.9%). It is our hope that
this information can be used to further the understanding
of the pathophysiology of syringomyelia formation and assist
in prenatal counseling and guide clinical management of
patients postnatally. The absence of a syrinx on fetal and
even early postnatal imaging is not a reliable indicator of
the likelihood of development of syringomyelia later in
life in this population.

Disclosure

The authors report no conflict of interest concerning the ma-
terials or methods used in this study or the findings specified in this
paper.

Author contributions to the study and manuscript preparation
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Fath, Bierbrauer. Acquisition of data: Bixenmann, Bansal. Analysis
and interpretation of data: Bixenmann, Kline-Fath, Bierbrauer.
Drafting the article: Bixenmann. Critical revisions of the article: all
authors. Reviewed submitted version of manuscript: all authors.
Approved the final version of the manuscript on behalf of all authors:
Bixenmann.

References

1. Adzick NS, Thom EA, Spong CY, Brock JW III, Burrows PK,
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