PATIENTS with Chiari I malformation either with or without syringomyelia often complain of headache and may experience syncope in association with coughing.10 The presence of the cerebellar tonsils within the foramen magnum apparently predisposes these patients to headache aggravated by cough. It has been proposed that syringomyelia in patients with Chiari I malformation results from occlusion of the free pulsatile movement of CSF across the foramen magnum during the cardiac cycle.2,5 Within this proposed mechanism, the tonsils create a partially entrapped spinal subarachnoid space. When the tonsils are forced downward in this partially enclosed, noncompliant space during systole, they cause high cervical subarachnoid pressure waves, which act externally on the spinal cord to enhance transmural movement of CSF into the spinal cord and to propel syrinx fluid with each heartbeat.2,5 Obstruction of the CSF pathways may also be important in the pathophysiology of headache associated with cough. In contrast to a slowly developing condition like syringomyelia, however, headache aggravated by cough is a transient symptom and its pathophysiology must be related to events of the cough, not the cardiac cycle.

A variety of physiological tests have been conducted to assess the degree to which CSF flow is impaired at the craniocervical junction by the Chiari I malformation. Specifically, measuring CSF pressure during the Queckenstedt test (jugular compression) and Valsalva maneuver has been used to determine the differential rates of increase in CSF pressure and the absolute CSF pressure in the intracranial space compared with that in the spinal subarachnoid space.2,5 Note, however, that the complete effect of jugular compression or the Valsalva maneuver on CSF pressure does not occur until several seconds after initiation. In contrast, coughing has an acute effect on CSF pressure. Because of its more rapid effect on CSF pressure, coughing may induce pressure changes that are more sensitive to obstruction of the rapid flow of CSF in the subarachnoid space than CSF pressure changes during the Queckenstedt test or Valsalva maneuver.

When examining CSF pressure during cough in patients with Chiari I malformation, several postulates can be made. Because the Chiari I malformation causes a partially enclosed spinal subarachnoid space with low compliance, one can theorize that the sudden increase in pressure in the spinal epidural veins during cough will produce an exaggerated CSF pressure response. Thus, the exaggerated response in these patients would indicate clinically significant obstruction to the free flow of CSF at the foramen magnum.
it is demonstrated that coughing produces exaggerated CSF pressure responses in patients with headache associated with cough, the headache itself may result from an abnormally high CSF pressure response.

We made the following hypotheses: 1) patients suffering from headache associated with cough have a greater elevation in intrathecal pressure during cough compared with either patients without headache or healthy volunteers; 2) after relieving the obstruction to the free flow of CSF at the foramen magnum by suboccipital craniectomy and duraplasty, peak subarachnoid pressure during cough decreases and is associated with relief of headache aggravated by cough; and 3) measurement of intrathecal pressure during cough is a more effective means of assessing obstruction of the free flow of CSF at the craniocervical junction than the Queckenstedt test or Valsalva maneuver.

Clinical Material and Methods

Between July 1994 and July 2001, 26 patients with Chiari I malformation and syringomyelia and four patients with Chiari I without syringomyelia underwent preoperative and postoperative subarachnoid pressure testing after being enrolled in a clinical research protocol, “Establishing the Physiology of Syringomyelia (NINDS 92-N-0226).” In addition, a group of 15 healthy adult volunteers were enrolled in a clinical research protocol, “Establishing Normal CSF Physiology to Allow Comparison With Syringomyelic CSF Physiology (NINDS 94-N-0160).” The Institutional Review Board of the NINDS approved the research protocols. Data gathered during compliance and Queckenstedt testing and Valsalva maneuver in 20 of 30 patients and the healthy volunteers in this study were included in a prior report in which the mechanism of syringomyelia was described.2 Note that data associated with coughing in these patients had not been evaluated until the writing of this paper.

Before and 6 months after surgery, the presence of headache associated with cough was determined by asking patients if coughing induced a headache. The extent of preoperative tonsillar herniation (millimeters below the foramen magnum) was also recorded.

Patients were evaluated before surgery by measuring the spinal subarachnoid pressure at L4–5 at baseline and during three to five coughs, jugular compression (Queckenstedt test, inflation of a cuff around the neck to 60 mm Hg for 10 seconds was used to compress the jugular veins3,11), and the Valsalva maneuver (patients blew into a tube at a constant pressure of 40 mm Hg). After these recordings were obtained, 10 ml of CSF was removed and pressure was noted again for measurement of compliance (milliliter of CSF per millimeter of mercury). Lumbar punctures were performed using fluoroscopic guidance and 22-gauge needles. Four days after this testing, patients underwent suboccipital craniectomy, C-1 laminectomy, and duraplasty. During surgery, intraoperative ultrasonography was used to visualize the Chiari I malformation and spinal cord at rest and during forced respiration (Valsalva maneuver). Six months after surgery, patients underwent reevaluation of spinal subarachnoid pressure at L4–5 at baseline and during three to five coughs, jugular compression, and Valsalva maneuver and after removal of 10 ml of CSF. These same evaluations were performed in the healthy volunteers only once. Values from this one session were compared with both preoperative and postoperative values obtained in patients (Tables 1 and 2).

Pressure data were recorded on the hard disk drive of a Macintosh computer (Apple Computer Inc., Cupertino, CA) by using Sorenson pressure transducers (Edwards Lifesiences, LLC, Irvine, CA) a physiological monitor, an

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**TABLE 1**

**Preoperative CSF physiological measurements***

<table>
<thead>
<tr>
<th>Intrathecal Pressure</th>
<th>Patients W/</th>
<th>Patients W/O</th>
<th>Healthy Volunteers</th>
</tr>
</thead>
<tbody>
<tr>
<td>during cough (mm Hg)</td>
<td>71.2 ± 26.7†</td>
<td>49.4 ± 15.6</td>
<td>52.7 ± 17.4</td>
</tr>
<tr>
<td>at baseline (mm Hg)</td>
<td>15.6 ± 4.1†</td>
<td>12.3 ± 2.8</td>
<td>11.0 ± 2.4</td>
</tr>
<tr>
<td>during compliance (ml/mm Hg)</td>
<td>2.3 ± 0.6‡</td>
<td>3.3 ± 2.0‖</td>
<td>6.4 ± 4.3</td>
</tr>
<tr>
<td>slope during cough (mm Hg/second)</td>
<td>171.3 ± 66.5</td>
<td>170.2 ± 80.9</td>
<td>211.8 ± 73.2</td>
</tr>
<tr>
<td>max value during Valsalva maneuver (mm Hg)</td>
<td>41.4 ± 11.3</td>
<td>38.6 ± 10.8</td>
<td>45.1 ± 7.4</td>
</tr>
<tr>
<td>slope during jugular compression (mm Hg/second)</td>
<td>4.0 ± 2.8‖</td>
<td>4.1 ± 2.3‡</td>
<td>6.6 ± 2.0</td>
</tr>
</tbody>
</table>

*All values are the means ± standard deviation.
†Value is significantly different from those in patients without headache associated with cough and in healthy volunteers.
‡Value is significantly different from that in healthy volunteers.

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**FIG. 1.** Scatterplot of peak intrathecal pressure during a cough in patients with or without headache associated with cough and in healthy volunteers. Bars indicate mean values.
analog-to-digital converter board, and Labview data acquisition software (National Instruments Corp., Austin, TX). Pressure transducers were calibrated with a static water column.

Pressure values obtained in patients before and after surgery were compared with those in healthy volunteers by using the unpaired Student t-test. In a separate analysis, preoperative values in patients were compared with postoperative values with the aid of the paired Student t-test. Analysis of variance together with the Fisher protected least-significant-difference method was used to determine if patients with headache aggravated by cough had more exaggerated CSF pressure responses to coughing than patients without headache and healthy volunteers. Linear regression analysis was performed to assess the correlation between different physiological parameters. A probability value of 0.05 or less was considered to be significant. All statistical analyses were performed using Statview software (SAS Institute, Inc., Cary, NC).

**Results**

**Preoperative Testing**

All four patients who had Chiari I malformation without syringomyelia suffered from headache associated with cough. Seven of 26 patients with Chiari I malformation and syringomyelia had headache aggravated by cough. Patients with headache associated with cough had the highest intrathecal pressure during coughing, a factor different in patients without headache and in healthy volunteers (analysis of variance, p = 0.008 and 0.04, respectively; Table 1 and Fig. 1). In contrast, in patients with Chiari I malformation but no headache associated with cough, the peak cough-induced CSF pressure was not different from normal values (p = 0.6). The slope (millimeters of mercury per second) of the increase in CSF pressure during cough was similar in patients with headache aggravated by cough, in patients without, and in healthy volunteers (p = 0.97, 0.1, 0.2, respectively). Patients with headache associated with cough also had the highest baseline intrathecal pressure, a factor different in patients without headache and in healthy volunteers (p = 0.02 and 0.002, respectively; Table 1). There was an inverse correlation between preoperative compliance values and peak intrathecal pressure values during cough (r = 0.3). Preoperative values obtained during compliance testing of the spinal subarachnoid space in patients (with or without headache) were significantly lower than those collected during compliance testing in healthy volunteers (p = 0.006 and 0.01, respectively). Note, however, that there was no significant difference in compliance between patients with and without headache (p = 0.1). Patients with headache associated with cough had similar intrathecal pressures during coughing regardless of whether they had syringomyelia (p = 0.5; Fig. 2).

The maximum value of intrathecal pressure during the Valsalva maneuver was obtained in all patients and healthy volunteers. There was no significant difference in peak pressure during the Valsalva maneuver comparing patients with and those without headache (p = 0.5). While performing the Valsalva maneuver, pressure in healthy volunteers was not significantly different from that in patients with and in those without headache (p = 0.3 and 0.06, respectively; Table 1).

The rate of the increase in intrathecal pressure during Queckenstedt testing was similar to that in patients with and without headache (p = 0.9). In both of these patient groups, however, the slope was less than that in healthy volunteers (p = 0.01 and 0.003, respectively). The correlation between

![Fig. 2. Scatterplot of peak intrathecal pressure during a cough in patients with Chiari I malformation (with or without syringomyelia) and in healthy volunteers.](image-url)
preoperative values of slope of intrathecal pressure during jugular compression and that during cough was low ($r = 0.09$).

The mean extent of tonsillar herniation in patients with headache associated with cough, in those without, and in healthy volunteers was $14.6 \pm 6.3$, $11.7 \pm 4.4$, and $0.4 \pm 1.1$ mm, respectively. The degree of tonsillar herniation, as measured by the distance of the tonsillar tips below the foramen magnum, was not significantly different in patients with or without headache aggravated by cough ($p = 0.1$).

Postoperative Testing

Postoperative physiological outcome variables were again analyzed in the three groups; patients with headache associated with cough, those without, and healthy volunteers (Table 2). Postoperative peak intrathecal pressure during coughing in patients with headache aggravated by cough, in those without, and in healthy volunteers were not significantly different from each other, as indicated by results of analysis of variance testing ($p = 0.1, 0.2$, and $0.5$, respectively). After surgery, the slopes of intrathecal pressure during coughing in patients with or without headache associated with cough were significantly lower than normal ($p = 0.002$ and $0.003$, respectively). Postoperative baseline intrathecal pressures in patients with headache exacerbated by cough, in those without, and in healthy volunteers were not significantly different from each other ($p = 0.7, 0.8$, and $0.8$, respectively). After surgery, compliance measurements of the spinal subarachnoid space in patients with or without headache associated with cough were not significantly different from those obtained in healthy volunteers ($p = 0.1$ and $0.3$, respectively). Postoperative values of intrathecal pressure obtained during the Valsalva maneuver were similar in patients with or without headache associated with cough ($p = 0.5$). Patients with headache had significantly lower peak intrathecal pressures during the Valsalva maneuver compared with pressures in healthy volunteers ($p = 0.02$). The rate of increase in intrathecal pressure during jugular compression in both patient groups was not different from that in healthy study participants ($p = 0.3$ and $0.2$, respectively).

Cough Physiology With Symptomatic Chiari I Malformation

Surgical decompression had a significant effect on symptoms 6 months after surgery, given that headache associated with cough resolved completely in 10 of 11 patients and improved in the remaining patient. To assess the overall effect of surgery in this population, patients were analyzed as a single group when comparing preoperative and postoperative parameters. Surgical decompression had a significant effect on all physiological measures associated with cough, as demonstrated by comparison of preoperative and postoperative values (Table 3). Intrathecal pressure during cough in all patients fell from $57.4 \pm 22.6$ mm Hg before surgery to $43.9 \pm 14.6$ mm Hg after surgery ($p = 0.001$, paired Student t-test; Figs. 3 and 4), and the slope of intrathecal pressure during cough diminished after surgery ($p = 0.01$). Baseline intrathecal pressure decreased ($p = 0.001$) and compliance of the spinal subarachnoid space increased ($p = 0.03$). The transmission of intrathecal pressure across the foramen magnum during jugular compression rose at an increased rate after surgery compared with that before surgery ($p = 0.004$). Peak intrathecal pressure during the Valsalva maneuver was the sole parameter unaltered by surgery ($p = 0.9$).

Discussion

Headache is a common symptom in patients with the Chiari I malformation, occurring in 15 to 75% of them. Patients with Chiari I malformations often complain of headaches for several years before their disease is diagnosed. In a recent study authors demonstrated that 17 (57%) of 30 patients whose chief complaint was headache associated with cough ultimately received the diagnosis of a Chiari I malformation. Thus, if the presence of headache exacerbated by cough is established in a patient’s history, there is a good chance that the patient has a symptomatic Chiari I malformation. Note that there are various forms of headache in this patient population. Some patients complain of a brief headache associated with coughing or straining, while others complain of headaches not precipitated by Valsalva-like maneuvers.

Mechanisms of Headache Associated With Cough as Proposed by Other Investigators

Few theories on the origin of headache aggravated by cough in patients with Chiari I have been proposed. In the report of Pascual, et al., 14 of 50 patients with Chiari I malformation had headache resulting from or aggravated by Valsalva-like maneuvers. In these 14 patients, the presence of headache correlated with the degree of tonsillar herniation. The authors attributed aggravation of the headache to compression of the C-1 and C-2 roots by further tonsillar herniation occurring during Valsalva-like maneuvers. In the

### TABLE 3

Comparison of preoperative and postoperative values in all patients

<table>
<thead>
<tr>
<th>Intrathecal Pressure</th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>during cough (mm Hg)</td>
<td>57.4 ± 22.6</td>
<td>43.9 ± 14.6</td>
<td>0.001</td>
</tr>
<tr>
<td>at baseline (mm Hg)</td>
<td>13.5 ± 3.7</td>
<td>10.7 ± 2.2</td>
<td>0.001</td>
</tr>
<tr>
<td>during compliance (ml/mm Hg)</td>
<td>3.0 ± 1.7</td>
<td>4.5 ± 3.3</td>
<td>0.03</td>
</tr>
<tr>
<td>slope during cough (mm Hg/second)</td>
<td>170.6 ± 75.0</td>
<td>134.2 ± 52.0</td>
<td>0.01</td>
</tr>
<tr>
<td>max value during Valsalva maneuver (mm Hg)</td>
<td>39.7 ± 10.9</td>
<td>39.5 ± 8.4</td>
<td>0.88</td>
</tr>
<tr>
<td>slope during jugular compression (mm Hg/second)</td>
<td>4.1 ± 2.4</td>
<td>8.5 ± 7.7</td>
<td>0.004</td>
</tr>
</tbody>
</table>
study reported here, however, we were unable to detect tonsillar descent using ultrasonography while performing Valsalva maneuvers during surgery. Therefore, it seems unlikely that the headache is dependent on tonsillar movement during the Valsalva maneuver.

Williams suggested that headache associated with cough results from craniospinal pressure dissociation. In his 1980 study, two patients suffering from headache aggravated by cough had cerebral ventricular and lumbar CSF pressures monitored during and after coughing and the Valsalva maneuver while they were seated in an upright position. Pressure was higher in the ventricle than in the intrathecal space after both Valsalva maneuver and coughing, leading Williams to postulate that a pressure differential associated with craniospinal pressure dissociation was the cause of headache linked to cough in these patients. Williams also detected craniospinal pressure dissociation in patients harboring Chiari I malformation without headache exacerbated by cough, and he did not compare patients with and without headache associated with coughing to see if they differed in degree of craniospinal pressure dissociation. Thus, Williams’ theory does not explain why some patients with Chiari I malformations have headache linked to coughing while others do not. Furthermore, data from our previous study of 20 patients with Chiari I malformation and syringomyelia showed that the Valsalva maneuver failed to produce significant pressure differentials between the intracranial and spinal subarachnoid spaces. Investigators in other studies have also failed to demonstrate significant craniospinal pressure differentials in patients with Chiari I malformations. These findings indicate that craniospinal pressure dissociation is an unlikely explanation for the cause of headache associated with cough in these patients. It is important to note that Williams’ patients were awake and seated in the upright position, whereas CSF pressure measurements in other studies were obtained in patients under anesthesia and in the prone position.

Proposed New Mechanism of Headache Associated With Cough

Our results suggest that the presence of headache associated with cough is related to the absolute value of spinal intrathecal pressure reached during a cough, and this elevated pressure is a sign of significant craniocervical CSF obstruction. In addition, our results indicate that headache arises because this obstruction produces elevated intracranial pressures and distention of the dura mater during coughing.

In this study, peak intrathecal pressure during cough was elevated in the group of patients suffering from headache associated with cough. Patients without headache had CSF pressures at baseline and during cough that were not significantly different from those in healthy volunteers. The physiological properties of coughing combined with partial entrapment of the CSF in the spinal subarachnoid space seems to explain the association of headache aggravated by cough with increased intrathecal pressure. During a cough, the brief increase in intrathoracic and intraabdominal pressure is transmitted through valveless veins to the epidural veins. The epidural veins distend as their pressure increases and transfer their pressure to the dura mater and subarachnoid space. Because the positioning of the tonsils produces a partially enclosed spinal subarachnoid space with low compliance in patients with Chiari I malformation, the sudden increase in pressure in the spinal epidural veins and the expansion of the veins during a cough produces an exaggerated CSF pressure response, as demonstrated in this study. From these results one can infer that patients with headache associated with cough had a higher degree of obstruction of the CSF space at the level of the foramen magnum than other patients, leading to elevated intrathecal pressures during a cough.

Intrathecal Pressure During Coughing as a Test for Obstruction of CSF Pathways

We sought to identify the physiological test that was the most sensitive measure of the degree of obstruction to movement of CSF in the subarachnoid space. In consideration of this it is noteworthy that during jugular compression, Valsalva maneuver, or measurement of compliance the CSF has several seconds to move across an area of partial obstruction, whereas only a fraction of a second is available during a cough. Thus, peak intrathecal pressure during coughing should be a more sensitive predictor of headache associated with cough and of partial obstruction of the CSF.
pathways at the foramen magnum (producing a partially enclosed spinal subarachnoid space) in these patients. Compliance values were significantly lower in patients compared with those in healthy volunteers, but this parameter did not distinguish the group of patients with from those without headache linked to cough. The slope of values of intrathecal pressure recorded during jugular compression was below normal levels in patients, but was an even less sensitive parameter than compliance testing in predicting which patients would have headache aggravated by cough. The Valsalva maneuver was not valuable in predicting headache associated with cough because it produced a similar rise in intrathecal pressure in patients with or without headache linked to cough. Of all these tests, the highest absolute pressures in the subarachnoid space occurred during coughing. A cough is a very acute, abrupt event, and high pressures develop in response to it because in symptomatic patients extreme narrowing of the CSF pathways at the craniocervical junction confines CSF. Thus, our results suggested that intrathecal pressure during coughing most strongly correlates with headache linked to cough and that of the physiological tests used in this study, it was the most effective measure to determine the degree of obstruction at the craniocervical junction.

Cough and Syringomyelia Pathophysiology

Headache associated with cough occurred in a higher proportion of patients harboring the Chiari I malformation alone compared with patients with both Chiari I malformation and syringomyelia. In patients with headache aggravated by cough, the intrathecal pressure during a cough was the same in patients with or without syringomyelia. Given that coughing occurs infrequently and transiently in patients, it is unlikely that elevated intrathecal pressure during the cough is related to the pathophysiology of syringomyelia. The episodic nature of a cough is in sharp contrast to the continuous, repetitive pulsation of CSF against the surface of the spinal cord, which occurs during the cardiac cycle, an elevated CSF pulse pressure that affects patients with the Chiari I malformation and syringomyelia.23

Effect of Craniocervical Decompression on Headache Associated With Cough and Intrathecal Pressure

Craniocervical decompression was highly effective in resolving the symptom of headache linked to coughing, completely relieving these headaches in 10 of 11 patients and partially relieving the headache in the remaining patient. Symptomatic improvement was accompanied by a reduction in peak intrathecal pressure during cough.

Conclusions

Patients with Chiari I malformation often complain of headache aggravated by cough for several years before the cause of the headache is diagnosed. Data from our study support the notion that the clinical symptom of headache linked to coughing is important to document when evaluating patients, because it can be used to determine the degree of occlusion of the CSF spaces at the craniocervical junction. We hope that the results of this study heighten the awareness of this unique clinical symptom, its physiological significance, and its effective relief with craniocervical decompression.

References


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Address reprint requests to: John D. Heiss, M.D., Surgical Neurology Branch, National Institutes of Health, 10 Center Drive, 10-5D37, MSC-1414, Bethesda, Maryland 20892-1414. email: heissj@ninds.nih.gov.