Pediatric hydrocephalus: systematic literature review and evidence-based guidelines. Part 2: Management of posthemorrhagic hydrocephalus in premature infants

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Object. The objective of this systematic review and analysis was to answer the following question: What are the optimal treatment strategies for posthemorrhagic hydrocephalus (PHH) in premature infants?

Methods. Both the US National Library of Medicine and the Cochrane Database of Systematic Reviews were queried using MeSH headings and key words relevant to PHH. Two hundred thirteen abstracts were reviewed, after which 98 full-text publications that met inclusion criteria that had been determined a priori were selected and reviewed.

Results. Following a review process and an evidentiary analysis, 68 full-text articles were accepted for the evidentiary table and 30 publications were rejected. The evidentiary table was assembled linking recommendations to strength of evidence (Classes I–III). Conclusions. There are 7 recommendations for the management of PHH in infants. Three recommendations reached Level I strength, which represents the highest degree of clinical certainty. There were two Level II and two Level III recommendations for the management of PHH.

Recommendation Concerning Surgical Temporizing Measures: I. Ventricular access devices (VADs), external ventricular drains (EVDs), ventriculosubgaleal (VSG) shunts, or lumbar punctures (LPs) are treatment options in the management of PHH. Clinical judgment is required. Strength of Recommendation: Level II, moderate degree of clinical certainty.

Recommendation Concerning Surgical Temporizing Measures: II. The evidence demonstrates that VSG shunts reduce the need for daily CSF aspiration compared with VADs. Strength of Recommendation: Level II, moderate degree of clinical certainty.

Recommendation Concerning Routine Use of Serial Lumbar Puncture: The routine use of serial lumbar puncture is not recommended to reduce the need for shunt placement or to avoid the progression of hydrocephalus in premature infants. Strength of Recommendation: Level I, high clinical certainty.

Recommendation Concerning Nonsurgical Temporizing Agents: I. Intraventricular thrombolytic agents including tissue plasminogen activator (tPA), urokinase, or streptokinase are not recommended as methods to reduce the need for shunt placement in premature infants with PHH. Strength of Recommendation: Level I, high clinical certainty.

Recommendation Concerning Nonsurgical Temporizing Agents: II. Acetazolamide and furosemide are not recommended as methods to reduce the need for shunt placement in premature infants with PHH. Strength of Recommendation: Level I, high clinical certainty.

Recommendation Concerning Timing of Shunt Placement: There is insufficient evidence to recommend a specific weight or CSF parameter to direct the timing of shunt placement in premature infants with PHH. Strength of Recommendation: Level I, high clinical certainty.

Recommendation Concerning Endoscopic Third Ventriculostomy: There is insufficient evidence to recommend the use of endoscopic third ventriculostomy (ETV) in premature infants with posthemorrhagic hydrocephalus. Strength of Recommendation: Level III, unclear clinical certainty.

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Key Words • hydrocephalus • infant • case management • posthemorrhagic hydrocephalus • premature infant • preterm infant • ventriculomegaly • intraventricular hemorrhage • meningitis • ventricular dilation • ventricular index • head circumference • in utero • shunt • reservoir • endoscopic third ventriculostomy • ventriculoperitoneal shunt • practice guidelines

Although reviews have been recently published, there exists a paucity of guidelines or evidence-based recommendations for the management of posthemorrhagic hydrocephalus (PHH) in infants. Ac-
Part 2: Management of posthemorrhagic hydrocephalus in infants

According to 2007 data provided by the Division of Vital Statistics of the Centers for Disease Control and Prevention (CDC), infants born with very low birth weight and gestational age have a significantly higher risk of mortality. In fact, more than 50% of all infant deaths in 2007 occurred in infants born before 32 weeks’ gestation. In 2008, the preterm birth rate declined for the second consecutive year to 12.3%, but this decrease primarily involved those infants born in the later preterm period (34–36 weeks). Low birth weight (LBW) also contributes to increased infant mortality, and the CDC has reported that the percentage of LBW infants, or infants born weighing less than 2500 g, increased by 24% between 1984 and 2006.

A recent study of 15,454 extremely low birth weight (ELBW) infants, each weighing between 401 g and 1000 g, was undertaken to assess neurodevelopmental outcome. More than 5000 infants died while in the hospital or before the follow-up visit. Among the 7693 children in whom follow-up studies were available, 2530 (33%) had a history of intraventricular hemorrhage (IVH). The IVH was Grade III or IV for 998 (13%) of the 7693 infants. Remarkably, in only 246 (3%) of the 7693 ELBW infants with follow-up was a shunt placed for PHH. There are still many questions about the optimal time to intervene for infants with PHH, and there are many different opinions about the best temporizing mechanism for symptomatic infans too small or unstable for permanent shunt placement.

The objective of this systematic review and analysis was to answer the following question: What are the optimal treatment strategies for posthemorrhagic hydrocephalus (PHH) in premature infants? We evaluated the current literature and constructed evidence-based recommendations supported by the strength of the available data for the management of PHH in premature infants. Specifically, we wanted to investigate relevant evidence for the following:

- Use of surgical temporizing methods such as ventricular reservoirs, external ventricular drains (EVDs), ventriculostubgaleal (VSG) shunts, and lumbar punctures (LPs).
- Routine use of serial LPs to reduce the need to shunt or to avoid the progression of hydrocephalus in premature infants.
- Use of intraventricular thrombolytic agents, including tissue plasminogen activator (tPA), urokinase, and streptokinase, to reduce the need for shunt placement in premature infants with PHH.
- Use of acetazolamide or furosemide to reduce the need for shunt placement in premature infants with PHH.
- Efficacy of endoscopic third ventriculostomy (ETV) in this population.
- Specific CSF parameters to direct the timing of shunt placement in premature infants with PHH.

Methods

Search Criteria

Both the US National Library of Medicine and the Cochrane Database of Systematic Reviews were queried using MeSH headings and key words relevant to PHH.


Strategy

Two hundred thirteen abstracts were reviewed, after which 98 publications that met the inclusion criteria were selected. In addition to the overall inclusion/exclusion criteria specified in the Methods section of the Guidelines (Part 1), additional inclusion criteria included studies in which infants younger than 12 months with all forms of hydrocephalus—both congenital and acquired—were evaluated to ensure that the maximum number of studies were reviewed. The analysis focused on studies evaluating infants with PHH because of the treatment strategies and challenges unique to this patient population.

As a result of the US National Library of Medicine’s search engine functionalities, additional search terms (heart ventricles) not relevant to topics addressed in this chapter were added to the search strategy. Although these search terms remained in the search strategy, we did not recall any references retrieved using them for full-text review. We excluded those references because they were not relevant to the overall scope of this project or the patient population addressed in this chapter and, therefore, did not meet the article inclusion criteria specified in the methodology section of this guideline (Part 1).

Following an evidentiary analysis and a review of the 98 full-text articles, 68 publications were accepted for inclusion in the evidentiary table and 30 publications were excluded. The evidentiary table was assembled linking recommendations to the strength of the evidence (Levels I–III).

Search Results

Of the 98 full-text articles selected for review, 30 full-text publications were rejected based on the criteria listed above and only 68 articles were used to construct the evidentiary table (Fig. 1). The criteria for the decision to treat were quite variable among different institutions and different study groups. For example, we evaluated 1 Class II study in which hydrocephalus was defined as the atrium of the lateral ventricle measuring > 10 mm on the horizontal plane of a head ultrasound (HUS) study or the body of the lateral ventricle at the level of the midthalamus measuring > 10 mm on a sagittal ultrasound image. We reviewed another Class III study in which hydroceph-
alas was defined as anterior cortical mantle thickness < 20 mm at an average postnatal age of 21 days along with increasing occipitofrontal circumference (OFC) as an indicator of hydrocephalus that should be treated. Bada et al. reported that of 10 infants requiring shunts, 5 (50%) experienced normal development, which was defined by physical and neurological assessment and evaluation using the Denver developmental screening tool. Evan’s ratio, which is described as the lateral measurement of the ventricle across the frontal horns divided by the lateral measurement across the brain (biparietal diameter; also known as the ventricular/biparietal [V/BP] ratio) can also be used to describe the severity of PHH. The majority of studies that were evaluated based on an initial diagnosis of PHH on HUS, CT, and MRI studies were also used. Choudhury described mild hydrocephalus as a V/BP ratio of 0.26–0.40, moderate hydrocephalus as a V/BP ratio of 0.40–0.60, severe hydrocephalus as a V/BP ratio of 0.60–0.90, and extreme hydrocephalus as a V/BP ratio of 0.91–1.0. These authors also reported that the thickness of the cortical mantle was not a statistically significant indicator of outcome because several infants with extreme hydrocephalus displayed normal motor development. One Class II and 1 Class III study indicated that when ventriculoperitoneal (VP) shunts were placed, even in cases of severe or extreme hydrocephalus, there were some infants with normal development and motor outcome (50 of 82 patients in the Choudhury study). Numerous studies have reported that good neurodevelopmental outcomes may be seen if and when infants with hydrocephalus are aggressively treated and cortical mantle thickness is restored.

Results

Surgical Temporizing Measures

RECOMMENDATION: Ventricular access devices (VADs), external ventricular drains (EVDs), ventriculosubgaleal (VSG) shunts, or lumbar punctures (LPs) are treatment options in the management of PHH. Clinical judgment is required. STRENGTH OF RECOMMENDATION: Level II, moderate degree of clinical certainty.

RECOMMENDATION: The evidence demonstrates that VSG shunts reduce the need for daily CSF aspiration compared with VADs. STRENGTH OF RECOMMENDATION: Level II, moderate degree of clinical certainty.

The evidence demonstrates that VADs reduce morbidity and mortality compared with EVDs. Three Class II and 7 Class III studies were included as evidence to support the first recommendation, and these lower-quality
studies documented the safety and efficacy of VADs, or Ommaya reservoirs, for the aspiration of CSF, ventricular decompression, and lowering of intracranial pressure. The authors of 2 Class II studies reported that ventricular reservoirs may reduce the incidence of shunt infection as well as noninfected shunt complications. In one Class II study and one Class III study, repeated aspiration of CSF from a VAD did not significantly increase the risk of infection. Three Class III studies reported that ventricular reservoirs did not significantly reduce the need for permanent shunt placement. One Class III study reported that the use of VADs, compared with the use of continuous ventricular drainage, significantly reduced morbidity and mortality rates that were associated with the surgical treatment of PHH in LBW infants with reservoirs, instead of EVDs (Table 1).

The placement of an EVD has also been used to treat hydrocephalus in preterm infants with PHH and is an option for these children, as shown in 1 Class II and 7 Class III studies. Three Class III studies reported that an EVD obviated the need for VP shunt placement in fewer than one-third of infants treated. More than 50% of preterm infants with PHH did require permanent VP shunt placement following removal of an EVD (95 out of 132 survivors required a shunt).

It has been reported that placement of a VSG shunt may reduce the need for permanent shunt placement. The authors of Class II and Class III studies reported trends toward shunt independence, but the studies only enrolled 32 and 95 patients, respectively, and the results were not statistically significant. In their report of a Class II, retrospective historical cohort study, Lam and Heilman demonstrated that VSG shunting significantly reduced the need for daily CSF aspiration, which may decrease the risk of introducing a de novo CSF infection. A chi-square test performed on their data indicated that a VSG shunt did significantly reduce the need for daily CSF aspiration when compared with a VAD ($\chi^2 = 19.2$, df = 1, $p = 0.000016$, $p < 0.05$). This may reduce the risk of infection or other complications. A larger, prospective study reported a statistically significant decreased need for permanent CSF diversion in infants treated with VSG shunts. This study reported that 66% of infants (20 of 30) treated with VSG shunts required VP shunts and 33% (10 of 30) remained shunt free; this was compared with a group of infants treated with VADs in which 75% (49 of 65) required VP shunts and only 25% of infants (16 of 65) remained shunt free.

In 2 studies, 1 intervention was compared to another with specific recommendations about the timing of the intervention for temporizing measures for the treatment of PHH in very LBW infants. In 1 Class III study, the authors compared early versus late intervention, as assessed by ventricular dilation in 5 collaborating neonatal centers. Ninety-five patients were subdivided into early intervention or late intervention groups, depending on their ventricular index at the time of initial treatment. Early treatment was safe and effective regardless of whether LP and/or reservoir placement was used. Early intervention was associated with a reduced requirement for a VP shunt (OR = 0.22) and reduced risk of moderate-to-severe disability. Additionally, there was a single Class III observational study of outcomes in which LPs, EVD, VSG shunts, and reservoirs were used. All interventional studies were found to be safe and effective.

### Routine Use of Serial Lumbar Puncture

**Recommendation:** The routine use of serial lumbar puncture (LP) is not recommended to reduce the need for shunt placement or to avoid the progression of hydrocephalus in premature infants. **Strength of Recommendation:** Level I, high degree of clinical certainty.

One Class I study was included, and it reported no statistical differences in outcomes of preterm infants with PHH treated with observation alone or infants treated with daily LP (Table 2). Lumbar puncture is often used early in the treatment of PHH, despite the fact that there is no statistically significant reduction in the need for a shunt or progression of PHH. In fact, LP neither predicts nor prevents the need for a permanent VP shunt. A second study, a Class III study, also reported no difference in adverse outcome regardless of whether infants were untreated or treated with serial LP. Without aggressive treatment of hydrocephalus and with persistent ventricular dilation, outcome was poor. Additionally, there was a single Class III study that concluded that repeated LPs may cause or contribute to subsequent shunt infection. Although LP may be useful for drawing off CSF as an immediate treatment for elevated intracranial pressure in infants with PHH, or for sampling CSF, we do not recommend the routine use of LP to eliminate the need for a VP shunt.

### Nonsurgical Temporizing Agents

**Intraventricular Thrombolytic Agents.** In Class II and Class III studies in which a decreased rate for the need for shunt placement in premature infants with PHH: Level I, high clinical certainty.

Based on 1 high-quality Class I study, the DRIFT procedure—DRainage, Irrigation, and Fibrinolytic Therapy (intraventricular tPA)—is not recommended for PHH. DRIFT did not significantly reduce shunt surgery or death, but it was associated with an increased rate of secondary IVH (Table 3). Forty-four percent (15 of 34) of infants in the DRIFT group died or required a shunt, compared with 50% (19 of 36) of infants who received standard treatment. Thirty-five percent (12 of 34) of preterm infants in the DRIFT study had secondary IVH, compared with 8% (3 of 34) who received standard treatment. These results differ from those of earlier Class II and Class III studies in which a decreased rate for the need for permanent shunt placement was reported when low-dose urokinase or fibrinolytic therapy with tPA was used for ventricular irrigation and clot reduction.

Reviews conducted by Whitelaw and Odd have also revealed that intraventricular injection of streptokinase has not been shown to be beneficial. A single case re-
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<td>Cornips et al., 1997</td>
<td>Retrospective review of 14 pts w/ Grade III or Grade IV IVH diagnosed on HUS study &amp; treated w/ EVD. 14 pts were compared w/ a historical cohort of 15 infants w/ similar Grade III/IV IVH.</td>
<td>Class II Retrospective review of 2 cohorts: premature infants treated w/ EVD vs those treated medically.</td>
<td>Ventricular drainage is a safe option for infants w/ PHH.</td>
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<td>Gurtner et al., 1992</td>
<td>Retrospective consecutively enrolled study of 736 LBW infants (&lt; 1500 g). After exclusion of some infants for various reasons, 547 infants were included in the retrospective consecutive review. Shunts were placed for progressive hydrocephalus &amp; OFC &gt; 95 percentile. 3 yrs of data examined by yr, by analyses of variance, &amp; Duncan’s mean comparison tests. Chi-square analyses on discrete variables such as rates of complication &amp; mortality. Student t-test w/ Bonferroni corrections. Spearman correlation coefficients were computed when appropriate. Quantitative data are presented.</td>
<td>Class II Consecutive, but not a randomized controlled study. A nonrandomized historical cohort, compared by yr of treatment &amp; treatment type. 1st yr: EVD. 2nd &amp; 3rd yr: subcutaneous reservoir was used. Outcomes evaluated: morbidity, mortality, &amp; need for shunt revision.</td>
<td>Frequency &amp; mortality of Grades III &amp; IV hemorrhage in infants weighing btwn 500 &amp; 700 g remained relatively constant over the 3-yr period. Authors concluded that there was a significant reduction in morbidity &amp; mortality associated w/ LBW infants when they began using reservoirs instead of EVDs.</td>
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<td>Hudgins et al., 1997</td>
<td>Use of urokinase via reservoir to treat PHH in 18 pts. 4 different doses of urokinase; ultimately grouped into “high” (n = 9) &amp; “low” dose (everyone else, n = 9). Both groups compared to historical control group w/ respect to outcome &amp; need for shunt. Prospective, case control.</td>
<td>Class II Prospective, nonrandomized, case-control series. Division of 9 pts into “low” dose group would appear to dilute statistical power despite statistical significance obtained. “Low dose” urokinase reduced shunt rate (71% vs 92%) compared to historical controls. Fewer shunt revisions in both groups compared to control group.</td>
<td>There was a trend toward VP shunt independence in the VSG shunt group, as compared to the VAD group, but it did not reach significance. VSG shunts decreased the need for daily taps. There was a slightly higher rate of complications in the VSG shunt group, but it was not significant.</td>
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<td>Lam &amp; Heilman, 2009</td>
<td>Single-institution, retrospective historical cohort study of 32 preterm infants w/ PHH. This study compared 2 cohorts of infants: those treated w/ VAD/Ommaya placement vs those treated w/ VSG shunts. There were no statistical differences in age or birth weight of the infants in the 2 groups. The groups were studied for IVH grade, need for daily CSF withdrawal, CSF leak from the scalp, CSF infection, &amp; need for a VP shunt.</td>
<td>Class II A chi-square test was performed ($\chi^2 = 19.2, df = 1, p = 0.000016, p &lt; 0.05$), which showed that VSG shunts significantly reduced the need for daily CSF aspiration compared to VADs. The higher rate of complications of VSG shunts was not statistically significant compared w/ the VAD group (p = 0.17). 93.75% (15 of 16 pts) in the VAD group required VP shunts while 71.42% (10 of 14 pts) in the VSG shunt group needed VP shunts. There was a trend toward VP shunt independence in the VSG shunt group, as compared to the VAD group, but it did not reach significance. VSG shunts decreased the need for daily taps. There was a slightly higher rate of complications in the VSG shunt group, but it was not significant.</td>
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<td>Anwar et al., 1986</td>
<td>Consecutive, nonrandomized study of 19 preterm infants w/ PHH who underwent placement of reservoirs for symptomatic hydrocephalus. Symptomatic hydrocephalus was defined as infants w/ rapidly increasing OFC, ventriculomegaly, &amp; signs of increased ICP present, such as tense fontanelle, splayed sutures, apnea, bradycardia, seizure, feeding difficulties, or lethargy.</td>
<td>Class III Study was a case series of infants weighing &lt;2000 g, w/ clear CSF &amp; treated w/ reservoirs. There was only limited presentation of qualitative &amp; quantitative data. Data included: morbidity, mortality, &amp; need for shunt placement in these infants. There was no comparison w/ a cohort of nontreated infants or infants treated w/ ventricular drains.</td>
<td>The authors concluded that reservoirs provide safe &amp; effective treatment for infants w/ PHH &amp; symptomatic hydrocephalus.</td>
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## TABLE 1: Surgical temporizing measures: summary of evidence* (continued)

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<td><strong>Benzel et al., 1993</strong></td>
<td>41 pts requiring ventricular drainage for hydrocephalus/PHH were evaluated retrospectively. All drainage procedures were performed on pts w/ IVH &amp; hydrocephalus (Grade III [25 pts]) &amp; pts w/ IVH &amp; IPH (Grade IV [16 pts]) in whom medical management had failed.</td>
<td>Class III Retrospective case series of 41 consecutive premature infants. 26 ventricular reservoirs (Rickham or McComb reservoirs) were placed in neonates weighing &lt;1500 g, allowing for safe but intermittent ventricular access. 18 of these reservoirs were subsequently converted to VP shunts. 32% of pts developed a VP shunt &amp;/or reservoir infection &amp; 59% required a shunt revision during the 1st yr of life. No Grade IV pts achieved normal functional level, while 10 Grade III pts did. The incidence of severe developmental delay (44% vs 28%) &amp; death (38% vs 12%) was greater in Grade IV than in Grade III pts.</td>
<td>Authors state, “The placement of ventricular reservoirs is acceptable as an alternative to early placement of ventriculo-peritoneal shunts. This approach may reduce the incidence of shunt infection as well as noninfectious shunt complications.”</td>
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<td><strong>Brouwer et al., 2007</strong></td>
<td>Single-center retrospective review of 76 preterm infants treated for PHVD w/ ventricular reservoirs. Infection rates were measured in 2 successive 6-yr intervals. No. of reservoir punctures also examined.</td>
<td>Class III Single-center retrospective review.</td>
<td>While the no. of reservoir punctures did not change, the infection rate was lower in the 2nd, more recent interval (2 of 50 pts [4%] vs 5 of 26 pts [19.2%]). Conclusion: Risks associated w/ ventricular reservoirs are w/in acceptable limits.</td>
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<td><strong>de Vries et al., 2002</strong></td>
<td>Retrospective review of consecutive preterm infants (EGA ≤34 wks) w/ Grade III IVH treated for posthemorrhagic ventricular dilatation in 5 collaborating NICUs (n = 95). Pts were subdivided into early intervention or late intervention groups, depending on their ventricular index at the time of initial treatment.</td>
<td>Class III Multicenter study, retrospective case series. Treatments were not standardized treatments. LPs, reservoir, &amp; shunt.</td>
<td>Early treatment was associated w/ a reduced requirement for VP shunt (OR = 0.22) &amp; reduced risk of moderate-to-severe disability.</td>
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<td><strong>Gaskill et al., 1988</strong></td>
<td>The use of a subcutaneous reservoir was studied in a consecutive, nonrandomized series of 38 infants w/ preterm IVH &amp; PHH. In all infants LP &amp; medical treatment had failed.</td>
<td>Class III Retrospective study of a series of premature infants who required temporizing measures (reservoir placement) after medical treatment/LP for PHH had failed. There were 28 survivors overall (8 died before a shunt could be placed, 2 died after shunt placement). 4 survivors (15%) did not require a shunt.</td>
<td>The authors concluded that early reservoir placement is a feasible, safe, &amp; effective treatment for PHH associated w/ preterm IVH.</td>
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<td><strong>Harbaugh et al., 1981</strong></td>
<td>Retrospective review of 11 premature infants w/ IVH &amp; PHH who were treated w/ tunneled EVD. The mean duration of drainage for this group was 20.7 days. No morbidity or mortality occurred as a result. 7 of 11 pts required a shunt. 2 of 11 did not require a VP shunt.</td>
<td>Class III Small retrospective case review.</td>
<td>EVD via a subcutaneously tunneled catheter was found to be a safe &amp; reliable initial method of treating PHH in premature infants.</td>
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<td>Heep et al., 2001</td>
<td>Safety/efficacy of Rickham reservoir placement for pts w/ PHH.</td>
<td>Class III Retrospective review. Broad inclusion criteria for reservoir placement. No comparison w/ pts managed w/ other methods.</td>
<td>Ommaya/Rickham reservoir is a safe, effective option for managing PHH until pt is ready for a shunt. 5% infection rate, 85% of pts needed a shunt.</td>
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<td>Hudgins et al., 1998</td>
<td>Use of VAD in 149 pts w/ PHH. Daily taps for 1st “several” days (10–15 cm³/kg).</td>
<td>Class III Single-institution retrospective case series. Shunts placed at 2 kg if pt was still symptomatic, but criteria not otherwise clear on when to stop VAD aspirations.</td>
<td>8% infection &amp; 20% revision rates. 88% shunt implantation rate.</td>
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<td>Kazan et al., 2005</td>
<td>Retrospective review of preterm &amp; LBW infants diagnosed w/ IVH by ultrasound (n = 42). 11 infants who required VP shunts were compared w/ 31 who did not. All pts received acetazolamide &amp; furosemide as an initial medical treatment.</td>
<td>Class IIISmall, single-center retrospective case series w/ grouping of pts despite variable treatments.</td>
<td>Risk factors for VP shunt included IVH grade, later EGA at birth, &amp; age (days) at time of IVH, but not treatment for IVH/PHH (acetazolamide, furosemide, LP, &amp; external ventricular drainage).</td>
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<td>Kormanik et al., 2010</td>
<td>Retrospective review of the outcome of infants receiving a ventricular reservoir for PHH.</td>
<td>Class IIIRetrospective observational study: a review of medical records of all infants who received a ventricular reservoir in 1 center between 2000 &amp; 2007.</td>
<td>35 ventricular reservoirs were placed. 6 pts (17%) were excluded. 29 pts had a total of 681 taps. There was no increased risk of infection from repeated or daily aspiration. Only 1 CSF culture-proven reservoir infection: Candida albicans.</td>
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<td>Kreusser et al., 1984</td>
<td>Study of 19 consecutive infants w/ PHH documented by CT or cranial ultrasound, &amp; ICP measurement by an indwelling ICP monitor. 5 of 19 pts were initially treated w/ LP, 30–40 ml CSF drained daily for 5–7 days. Surviving pts were evaluated w/ the Bayley Scale of Infant Development, the Cartell Infant Intelligence Scale, or the Stanford-Binet Intelligence Test, based on the child’s age at evaluation. Developmental quotient (DQ) was determined using the Denver Developmental Screening Test.</td>
<td>Class III Case series of a group of 19 consecutive infants treated w/ external ventricular drainage. There was no randomization to treat or not treat, &amp; no randomization of type of treatment. There was no case-controlled comparative cohort or group.</td>
<td>External ventricular drainage decreased ventricular size. 3 infants did not develop recurrent hydrocephalus &amp; did not require a shunt. 16 infants suffered recurrent hydrocephalus, w/in 1 wk after drain removal. Another EVD was placed in 10 pts. Following repeated EVDs, 9 of the 10 infants were stable enough for a shunt. The authors conclude that EVD is a safe &amp; effective treatment for PHH.</td>
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<td>Limbrick et al., 2010</td>
<td>Large single-center retrospective review of 325 preterm infants w/ grade III or IV IVH. The development of PHH &amp; the need for a temporizing device (VAD or VSG shunt) were studied. Infections, complications, &amp; need for VP shunt were analyzed, as was the mortality rate.</td>
<td>Class III Retrospective analysis showed 75.4% of the 65 infants treated w/ VAD needed a shunt; 66.7% of the 30 treated w/ VSG shunts required a shunt. There was no significant difference in the infection rate between VAD &amp; VSG shunts, revision rate, or VP shunt infection afterwards.</td>
<td>There was no significant difference in outcome between infants treated w/ VAD or VSG shunts.</td>
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<td>Rahman et al., 1993</td>
<td>Single-institution, small retrospective review of 37 pts w/ PHH, 31 of whom required VP shunt.</td>
<td>Class III Observational study of outcomes. LP, EVD, VSG shunts, &amp; Ommaya reservoirs were used. No statistical data available.</td>
<td>Suggested LP, VSG, Ommaya reservoir, &amp; VP shunts are safe &amp; effective for treating infants w/ PHH &amp; may obviate the need for further treatment.</td>
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<td>Rhodes et al., 1997</td>
<td>Study of 27 consecutive infants w/ PHH who had PHH &amp; increased ICP &amp; were treated w/ a tunneled EVD. PHH was defined as ventricular dilation, progressively increasing OFC, bulging fontanelle, widening of the sutures, apnea, or bradycardia.</td>
<td>Class III The study is a case series report.</td>
<td>PHH was successfully treated in all pts; the EVD was left in situ for an average of 23 ± 9 days. 4 pts died of unrelated causes &amp; 23 pts survived. 16 required shunts. Neurological outcome correlated w/ severity of the Grade of IVH. Grade IVH infants had the worst neurological outcome, despite treatment. The authors conclude that EVD is a safe &amp; effective treatment for PHH in premature infants.</td>
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<td>Weninger et al., 1992</td>
<td>Study of 31 premature infants w/ PHH who had PHH &amp; increased ICP &amp; were treated w/ a tunneled EVD.</td>
<td>Class III The study is a case series report.</td>
<td>PHH was successfully treated in all pts; the EVD was left in situ for an average of 23 ± 9 days. 4 pts died of unrelated causes &amp; 23 pts survived. 16 required shunts. Neurological outcome correlated w/ severity of the Grade of IVH. Grade IVH infants had the worst neurological outcome, despite treatment. The authors conclude that EVD is a safe &amp; effective treatment for PHH in premature infants.</td>
</tr>
<tr>
<td>Willis et al., 2009</td>
<td>Retrospective, consecutive case series of 32 infants who needed treatment for PHH. Multivariate analysis &amp; time series were used to identify factors that influence the outcome in terms of shunt revisions.</td>
<td>Class III</td>
<td>Initially reservoirs were placed in 46.8% of pts &amp; shunts in 53% of pts. The groups were not comparable. Permanent shunts were needed in 90.6% of cases. Infants who were treated w/ a shunt initially had more revisions. p = 0.0027. CSF reservoirs are a safe &amp; effective method of treatment in infants considered too small for VP shunt placement, but this does not obviate the need for a shunt.</td>
</tr>
<tr>
<td>Yu et al., 2009</td>
<td>The authors performed a retrospective case study of 11 premature infants w/ PHH who were all treated w/ a subcutaneous reservoir for CSF aspiration.</td>
<td>Class III Retrospective case series.</td>
<td>The authors concluded that CSF reservoir treatment is safe &amp; effective for infants w/ PHH.</td>
</tr>
</tbody>
</table>

EGA = estimated gestational age; ICP = intracranial pressure; IVH = intraventricular hemorrhage; NICU = neonatal intensive care unit; pts = patients.

* EGA = estimated gestational age; ICP = intracranial pressure; VP = ventriculoperitoneal; EVD = external ventricular drain; VSG = ventriculostomy; Ommaya reservoir = subcutaneous reservoir; PHH = posthemorrhagic hydrocephalus.
port of intravenous streptokinase, published in 1998, suggested that there may be some benefit.45 This report was followed by an early Class III study that found benefit in a nonrandomized cohort of preterm infants with PHH who were treated with intravenous low-dose streptokinase.46 However, data from a later Class II study led to the conclusion that routine use of intraventricular streptokinase in PHH was not recommended.79 These studies were included in the 2007 Whitelaw and Odd Cochrane review,24 which argues against intravenous streptokinase for the treatment of PHH in preterm infants (Table 3).

Despite increased short-term morbidity and recurrent IVH, some benefits were noted in the DRIFT survivors.72 In the most recent Whitelaw study,72 the reduction in the primary long-term outcome—death or severe disability—at 2 years in the DRIFT group reached statistical significance when adjusted for sex, birth weight, and grade of IVH. Severe cognitive disability also was reduced, and this improvement in cognitive function was statistically significant. There was also a reduction in severe sensorimotor disability with DRIFT, but this clinical improvement did not reach statistical significance. The authors hypothesized that the greater effect on cognitive rather than sensorimotor function may be attributed to paren-

### Table 2: Serial lumbar punctures: summary of evidence

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Study Description</th>
<th>Data Class, Quality, &amp; Reasons</th>
<th>Results &amp; Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anwar et al., 1986</td>
<td>Randomized controlled study of 47 consecutive preterm infants with PHH &amp; Grade III or Grade IV IVH. Infants enrolled in the study were randomized to observation only or daily LP. Cohorts were studied for morbidity, mortality, &amp; need for a shunt.</td>
<td>Class I Consecutively enrolled infants randomized to treatment (daily LP) (n = 24) or observation only (n = 23). 10 of 24 infants treated w/ LP required shunts &amp; 9 of 23 infants in the observation-only group required shunt placement for progressive PHH &amp; hydrocephalus.</td>
<td>There were no statistical differences in outcomes studied in infants treated w/ observation alone &amp; infants treated w/ daily LP. Although LP was safe, there was no statistically significant reduction in the need for shunt or progression of PHH.</td>
</tr>
<tr>
<td>Behjati et al., 2011</td>
<td>Case series study that investigated risk factors for VP shunts in infants w/ hydrocephalus following IVH in 97 consecutive preterm infants w/ IVH.</td>
<td>Class III Case series of 97 infants w/ IVH associated w/ prematurity. Risks factors associated w/ need for a shunt were investigated. Infants were followed for 1 yr. Morbidities &amp; mortalities were reported in a quantitative fashion. Pts treated medically w/ acetazolamide showed no benefit; however, infants treated w/ repeated CSF drainage through LP did have a higher shunt infection rate once the shunts were placed.</td>
<td>Infants w/ Grade III or IV IVH are at the highest risk of PHH &amp; hydrocephalus. 11 of 31 pts who required a shunt developed shunt infection, which was significantly associated w/ repeated LPs.</td>
</tr>
<tr>
<td>Chaplin et al., 1980</td>
<td>Retrospective review of 22 consecutive LBW infants w/ PHH. All pts developed hydrocephalus after 2 wks of age. The first 12 required VP shunts. In 10 infants born after September 1974, an attempt was first made to control the hydrocephalus w/ repeated LPs &amp; diuretics prior to placing a shunt. In 7 of 10 pts hydrocephalus was successfully arrested by medical therapy alone.</td>
<td>Class III Retrospective review of 22 infants w/ PHH. There were 2 cohorts: 12 pts treated w/ VP shunt, &amp; 10 pts treated w/ LP &amp; diuretics.</td>
<td>Follow-up when pt was 1–8 yrs of age in 18 infants. 2 of 12 pts treated w/ permanent shunts &amp; 3 of 6 pts treated medically had IQ scores ≥85. These results indicate a poor long-term outlook for the LBW infant who develops clinically overt hydrocephalus after intracranial bleeding.</td>
</tr>
<tr>
<td>Kazan et al., 2005</td>
<td>Single-center retrospective review of preterm &amp; LBW infants w/ IVH diagnosed by ultrasonography (n = 42). 11 infants who required VP shunts were compared w/ 31 who did not. All pts received acetazolamide &amp; furosemide as an initial medical treatment.</td>
<td>Class III Small, retrospective case series w/ grouping of pts despite variable treatments.</td>
<td>Risk factors for VP shunt included IVH grade, later EGA at birth, &amp; age (days) at time of IVH, but not treatment for IVH/PHH (acetazolamide, furosemide, LP, or external ventricular drainage).</td>
</tr>
<tr>
<td>Müller et al., 1998</td>
<td>Effect of aggressive LP schedule on PHH. LPs started at 0–4 days; on average 11 LPs performed per pt, 15 ml/kg or end of CSF flow per LP. Used protein, red blood cell count, glucose, &amp; ventricle size to determine end point.</td>
<td>Class III Single-institution nonrandomized prospective study. 16% complete resolution, 65% ventriculomegaly but no shunts, 19% w/ shunts.</td>
<td>Serial LP should be started early for treatment of hydrocephalus.</td>
</tr>
</tbody>
</table>
Part 2: Management of posthemorrhagic hydrocephalus in infants

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Study Description</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Whitelaw et al., 2007</td>
<td>Randomized multicenter clinical trial comparing standard treatment to DRIFT. 70 infants enrolled (34: DRIFT; 36: standard treatment). Outcomes: pts at 6 mos of age or at hospital discharge: death or VP shunt surgery, secondary IVH, &amp; infection.</td>
<td>Class I Multicenter randomized controlled trial.</td>
<td>15 of 34 pts (44%) in the DRIFT group died or required a shunt, compared w/ 19 of 36 pts (50%) who received standard treatment. 12 of 34 pts (35%) in DRIFT group had secondary IVH compared w/ 8% of pts who received standard treatment. Conclusion: DRIFT did not reduce shunt surgery or death but was associated w/ an increased rate of secondary IVH.</td>
</tr>
<tr>
<td>Hudgins et al., 1997</td>
<td>Use of urokinase via reservoir to treat PHH in 18 pts. 4 different doses of urokinase; pts ultimately grouped into &quot;high&quot; (n = 9) &amp; &quot;low&quot; dose (everyone else, n = 9). Both groups compared to historical control group w/ respect to outcome &amp; need for shunt. Prospective, case control.</td>
<td>Class II Prospective nonrandomized case-control series.</td>
<td>&quot;Low dose&quot; urokinase reduced shunt rate (71% vs 92%) compared to historical controls. Fewer shunt revisions in both groups compared to control group.</td>
</tr>
<tr>
<td>Whitelaw &amp; Odd, 2007</td>
<td>Review &amp; meta-analysis of 2 prospective case-control studies (Luciano et al., 1997 &amp; Yapicioğlu et al., 2003). Both source studies included total of 12 pts: 6 cases, 6 controls. Meta-analysis.</td>
<td>Class II Both sources’ studies were Class II (both were small randomized, prospective case-control studies).</td>
<td>No difference in mortality or VP shunt rate was observed w/ intraventricular streptokinase. Intraventricular fibrinolytic therapy cannot be recommended for infants following IVH.</td>
</tr>
<tr>
<td>Yapicioğlu et al., 2003</td>
<td>Single-blind prospective study. 12 preterm infants who developed PHH were randomly assigned to the control group (no treatment) or to receive intraventricular streptokinase (&gt;3 days). Note: the streptokinase group also had an LP (10–15 ml) prior to treatment &amp; then daily LPs (5–10 ml). They also received intraventricular vancomycin. Primary outcome: VP shunt placement.</td>
<td>Class II Small randomized, prospective study</td>
<td>5 of 6 infants in the streptokinase group &amp; 3 of 6 in the control group required VP shunts. No complications were noted. Routine use of intraventricular streptokinase in PHH was not recommended.</td>
</tr>
<tr>
<td>Richard et al., 2001</td>
<td>Single-institution experience w/ Ommaya reservoir in 64 pts. 17 pts received fibrinolytic therapy through Ommaya reservoir.</td>
<td>Class III Retrospective case series. Statistics performed on fibrinolytic therapy subgroup, which consisted of 2 different agents w/ multiple doses. Fibrinolytic subgroup then mixed back into overall outcome analysis.</td>
<td>Fibrinolytic therapy led to statistically significant lower rate of shunt placement (31% vs 87%).</td>
</tr>
<tr>
<td>Whitelaw et al., 2003</td>
<td>Prospective Phase I trial of new treatment methodology (DRIFT) for prevention of PHH of prematurity. Data from 24 pts compared w/ historical controls. Outcome measures: death, need for shunt, secondary IVH, infection, &amp; neurodevelopmental outcome.</td>
<td>Class III Prospective Phase I trial in 24 pts &amp; compared w/ historical controls.</td>
<td>1 pt died. 17 of 23 (74%) did not require a shunt. 2 pts experienced secondary IVH, &amp; 2 experienced infections. 19 pts &gt;12 mos had neurodevelopmental testing: 8 (42%) were normal; 7 (37%) had a single disability; 4 (21%) had multiple disabilities. Conclusion: Compared w/ historical controls, DRIFT reduced the need for shunts &amp; showed a trend toward lower rates of mortality &amp; disability.</td>
</tr>
</tbody>
</table>

(continued)
Chyromal infarction in the periventricular white matter, which was seen in about half of the infants enrolled in the trial.72

**Acetazolamide and Furosemide.** Recommendation: Acetazolamide and furosemide are not recommended as methods to reduce the need for shunt placement in premature infants with PHH. Strength of Recommendation: Level I, high clinical certainty.

After our review of the literature, we found two Class I studies that reported that preterm infants with a diagnosis of PHH who were treated with acetazolamide and furosemide demonstrated higher risks of neurological complications, morbidity, and mortality (Table 4).34,37 The International Posthemorrhagic Ventricular Dilation (PHVD) Drug Trial Group reported that administration of acetazolamide plus furosemide leads to higher rates of shunt placement (relative risk 1.42) and morbidity (84% vs 60%) compared with standard therapy.34 Kennedy et al.37 reported that treatment of PHVD with acetazolamide and furosemide did not decrease the rate of shunt placement (64% in the acetazolamide/furosemide group vs 52% in the control group, not treated with acetazolamide/furosemide).37 However, treatment was associated with an

### TABLE 3: Intraventricular thrombolytic agents: summary of evidence (continued)

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Study Description</th>
<th>Data Class, Quality, &amp; Reasons</th>
<th>Results &amp; Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whitelaw et al., 1992</td>
<td>Prospective study of 9 preterm infants w/ progressive posthemorrhagic ventricular dilation who underwent a 48- to 72-hr continuous intraventricular infusion of streptokinase. Outcomes: death, need for shunt, secondary IVH.</td>
<td>Class III Small, prospective, nonrandomized cohort study (Phase I trial).</td>
<td>All pts survived; only 1 of 9 required a shunt prior to discharge (later reports indicated that a total of 4 of 9 ultimately required shunts). No infections, 1 repeat hemorrhage.</td>
</tr>
<tr>
<td>Whitelaw et al., 1996</td>
<td>Phase I study to evaluate safety of tPA in 22 preterm infants w/ posthemorrhagic ventricular dilation. Dose-finding data reported. Outcome measures: death &amp; need for shunt prior to discharge &amp; secondary IVH.</td>
<td>Class III Small, prospective, nonrandomized cohort study (Phase I trial).</td>
<td>Dose-finding &amp; pharmacokinetic data reported ([tPA], half-life tPA). 21 (95%) of 22 pts survived. 9 (43%) of 21 pts required shunts. 1 pt experienced secondary IVH. Conclusion: tPA resulted in survival w/o shunt in most pts.</td>
</tr>
</tbody>
</table>

### TABLE 4: Acetazolamide/furosemide: summary of evidence

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Study Description</th>
<th>Data Class, Quality, &amp; Reasons</th>
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</tr>
</thead>
<tbody>
<tr>
<td>International PHVD Drug Trial Group, 1998</td>
<td>Use of acetazolamide &amp; furosemide in pts w/ PHH. Comparison w/ standard therapy for shunt placement &amp; neurological outcome.</td>
<td>Class I Randomized controlled multicenter, well designed.</td>
<td>Acetazolamide &amp; furosemide led to higher rates of shunt placement (RR 1.42) &amp; higher morbidity (84% vs 60%) compared w/ standard therapy</td>
</tr>
<tr>
<td>Kennedy et al., 2001</td>
<td>Multicenter randomized controlled trial designed to test the hypothesis that treatment of PHVD w/ acetazolamide &amp; furosemide (vs standard therapy) would reduce: 1) risk of shunt placement or death before 1 yr; &amp; 2) death or disability at 1 yr. 177 pts recruited from 55 centers worldwide.</td>
<td>Class I Multicenter randomized controlled trial. Positive: Excellent subject retention. Therapeutic CSF removal in 56% of pts (equivalent in both groups). Negative: Acetazolamide &amp; furosemide administration was stopped in many pts due to adverse effects. Also, furosemide was given in the standard therapy group in some cases.</td>
<td>Treatment of PHVD w/ acetazolamide &amp; furosemide did not decrease the rate of shunt placement (64% in acetazolamide/furosemide group vs 52% in the control group, not treated with acetazolamide/furosemide). Authors concluded: “Treatment of PHVD w/ acetazolamide &amp; furosemide cannot be recommended.”</td>
</tr>
<tr>
<td>Kazan et al., 2005</td>
<td>Single-center retrospective review of preterm &amp; LBW infants diagnosed w/ IVH by ultrasonography (n = 42). 11 infants who required VP shunts were compared w/ 31 infants who did not. All pts received acetazolamide &amp; furosemide as an initial medical treatment.</td>
<td>Class III Small retrospective case series w/ grouping of pts despite variable treatments.</td>
<td>Risk factors for VP shunt included IVH grade, later EGA at birth, &amp; age (days) at time of IVH, but not treatment for IVH/PHH (acetazolamide, furosemide, LP, or external ventricular drainage).</td>
</tr>
</tbody>
</table>

* RR = relative risk.
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increased rate of neurological morbidity (81% vs 66%).37 Treatment of PHVD with acetazolamide and furosemide was not recommended.37 One Class III study reported this treatment was not associated with VP shunt placement, but the severity of IVH (based on IVH grade) and the patient age at the time of IVH were significantly associated with the need for permanent CSF diversion.36 Kennedy et al. also noted that the ventricular index at time of entry into trial was the only factor significantly predictive of death or need for shunt, after multiple logistic regression analysis.37

Timing of Shunt Placement

**Strength of Recommendation:** There is insufficient evidence to recommend a specific infant weight or CSF parameter to direct the timing of shunt placement in premature infants with PHH. **Strength of Recommendation:** Level III, unclear degree of clinical certainty.

There were two Class III studies which evaluated the lower limits of infant weight at time of initial shunt insertion (Table 5).2,8 A weight of 1500 g was safely used as a criterion for VP shunt placement in the Benzel study.8 A single Class III study showed that CSF cell count, protein, and glucose levels were not statistically related to the occurrence of shunt failure or infection in the study population.24 The authors recommended that placement of the shunt be timed when the infant’s age, weight, and overall stability allow.24

**Endoscopic Third Ventriculostomy**

**Recommendation:** There is insufficient evidence to recommend the use of endoscopic third ventriculostomy (ETV) in premature infants with PHH. **Strength of Recommendation:** Level III, unclear degree of clinical certainty.

Although ETV was discussed in several full-text ar-

### TABLE 5: Timing of shunt placement—specific weight or CSF parameter: summary of evidence

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
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<th>Results &amp; Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anwar et al., 1986</strong></td>
<td>Consecutive, nonrandomized study of 19 preterm infants w/ PHH who underwent placement of reservoirs for symptomatic hydrocephalus. Symptomatic hydrocephalus was defined as presence of rapidly increasing OFC, ventriculomegaly, &amp; signs of increased ICP, such as tense fontanelle, splayed sutures, anemia, bradycardia, seizure, feeding difficulties, or lethargy.</td>
<td>Class III</td>
<td>Authors concluded that reservoirs provide safe &amp; effective treatment for infants w/ PHH &amp; symptomatic hydrocephalus.</td>
</tr>
<tr>
<td><strong>Benzel et al., 1992</strong></td>
<td>41 pts requiring ventricular drainage for hydrocephalus/PHH were evaluated retrospectively. All drainage procedures were performed in pts w/ IVH &amp; hydrocephalus (Grade III [25 pts]) &amp; in pts w/ IVH &amp; IPH (Grade IV [16 pts]) in whom medical management failed. 26 ventricular reservoirs were placed in neonates weighing &lt;1500 g; 18 of these reservoirs were subsequently converted to VP shunts.</td>
<td>Class III</td>
<td>Authors endorse reservoirs as an alternative to early shunts &amp; report that this strategy may reduce the incidence of shunt infection as well as noninfectious shunt complications. There was a VP shunt &amp;/or reservoir infection in 32% of pts. 59% of pts required a shunt revision during the 1st yr of life. No Grade IV pts achieved normal functional level, while 10 Grade III pts did. The incidence of severe developmental delay (44% vs 28%) &amp; death (38% vs 12%) was greater in the Grade IV than in Grade III pts.</td>
</tr>
<tr>
<td><strong>Fulkerson et al., 2011</strong></td>
<td>Premature infants w/ PHH have a high risk of shunt obstruction &amp; infection. Risk factors for complications include grade of IVH &amp; age at shunt insertion. There is anecdotal evidence that the amount of red blood cells or protein levels in the CSF may also increase shunt complications. This study examined whether any relationship exists between CSF constituents &amp; shunt malfunction or infection.</td>
<td>Class III</td>
<td>Authors concluded that neither CSF cell count nor protein or glucose levels were statistically related to the occurrence of shunt failure or infection in the study population. The authors recommend that placement of the shunt be timed when weight, age, &amp; the overall stability of the infant allow.</td>
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</table>

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articles that we reviewed, there was insufficient evidence available for us to make a recommendation for or against its use for the treatment of PHH in premature infants (Table 6). Endoscopic third ventriculostomy for the treatment of hydrocephalus in infants and children will be discussed more thoroughly in subsequent chapters (in particular, Part 4).

**Excluded Studies**

We excluded 1 Class III study for low “preterm” patient representation (7 patients); in the review of 52 consecutive ETV procedures in 49 infants with hydrocephalus, most infants (31 patients) had aqueductal stenosis. Of the 7 infants with preterm PHH, 6 required a shunt even after ETV. Infants with PHH from premature birth did not benefit from ETV. We excluded another Class III study including patients with different etiologies for hydrocephalus. Although ETV was successful in 57% of patients (8 of 14), the majority of those infants had congenital aqueductal stenosis without PHH. In the remaining 6 patients, a VP shunt was needed. In 1 Class III single-institution retrospective case series, 18 preterm infants with PHH were treated initially with Ommaya reservoir placement: 1 patient died, 5 patients received a VP shunt, and 9 patients underwent ETV. Three patients did not require any further intervention. While overall, 59% were shunt free at the last follow-up, 5 of the 9 patients who were treated with ETV had to undergo repeated surgery for VP shunt placement. The authors recommended combining placement of an Ommaya reservoir with ETV to reduce shunt dependency for preterm infants with PHH. There was a large (101 patients) Class III multicenter, retrospective study evaluating the success rate of ETV in patients with hydrocephalus from subarachnoid hemorrhage, IVH, and/or CSF infection; a minority of the patients (25% [25 of 101]) had PHH of prematurity. Overall, ETV was successful in 52% of the infants with PHH of prematurity. Endoscopic third ventriculostomy was successful in 100% (13 of 13) of children with a his-

**TABLE 6: Endoscopic third ventriculostomy for PHH in premature infants: summary of evidence**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Elgamal et al., 2011</td>
<td>Review of 52 consecutive ETV procedures in 49 infants w/ hydrocephalus not necessarily associated w/ preterm IVH. Most infants (n = 31) had aqueductal stenosis. The remaining infants w/ hydrocephalus had other causes for it including Chiari II, Dandy-Walker cysts, quadrigeminal lipoma, &amp; cerebellopontine angle arachnoid cyst. Only 6 pts had PHH caused by preterm IVH.</td>
<td>Class III</td>
<td>Authors concluded that the success rate of 69.4% indicates that ETV is safe &amp; effective in infants w/ hydrocephalus not associated w/ PHH &amp; prematurity.</td>
</tr>
<tr>
<td>Lipina et al., 2008</td>
<td>Retrospective consecutive case series of 14 infants &lt;6 mo of age presenting w/ obstructive hydrocephalus. 8 of 14 pts had PHH. ETV was considered successful when a VP shunt was not necessary.</td>
<td>Class III</td>
<td>ETV was successful in 57% of pts—the majority of them w/ primary aqueductal stenosis. In the remaining 6 pts, a VP shunt was needed.</td>
</tr>
<tr>
<td>Peretta et al., 2007</td>
<td>Single-institution retrospective review of 18 consecutive preterm infants w/ PHH. Pts were treated w/ placement of an Ommaya reservoir for temporizing ventricular decompression. When necessary, pts later underwent VP shunt placement (n = 5) or ETV (n = 9).</td>
<td>Class III</td>
<td>Recommended combining Ommaya placement w/ ETV. It reduces shunt dependency in this condition.</td>
</tr>
<tr>
<td>Siomin et al., 2002</td>
<td>Multicenter retrospective case series of 101 pts who underwent ETV for hemorrhage or infection. Both pediatric &amp; adult pts included. Of the 101 pts, 25 were treated for PHH of prematurity, &amp; specific data were reported for this cohort. Successful ETV was defined as no further hydrocephalus operations required.</td>
<td>Class III</td>
<td>ETV was successful in 52% of pts w/ PHH of prematurity. Note: ETV was successful in 13 of 13 of pts w/ PHH who were previously treated w/ a shunt, whereas it was unsuccessful in 12 of 12 pts treated w/ ETV as the first-line treatment. ETV was not successful in pts w/ both hemorrhage &amp; infection.</td>
</tr>
</tbody>
</table>
tory of preterm PHH, even though these patients were initially treated with a shunt. Endoscopic third ventriculostomy was unsuccessful in 12 of 12 infants treated with ETV as the first-line treatment, following preterm PHH. In patients with both hemorrhage and infection, ETV was not successful.65

Conclusions

Surgical Temporizing Measures

Recommendation: Ventricular access devices (VADs), external ventricular drains (EVDs), ventriculosubgaleal (VSG) shunts, or lumbar punctures (LPs) are treatment options in the management of posthemorrhagic hydrocephalus (PHH). Clinical judgment is required. Strength of Recommendation: Level II, moderate degree of clinical certainty.

Recommendation: The evidence demonstrates that VSG shunts reduce the need for daily CSF aspiration compared with VADs. Strength of Recommendation: Level II, moderate degree of clinical certainty.

The evidence demonstrates that VADs reduce morbidity and mortality compared with EVDs.

Routine Use of Serial Lumbar Punctures

Recommendation: The routine use of serial lumbar puncture (LP) is not recommended to reduce the need for shunt placement or to avoid the progression of hydrocephalus in premature infants. Strength of Recommendation: Level I, high clinical certainty.

Nonsurgical Temporizing Measures

Recommendation: Intraventricular thrombolytic agents including tissue plasminogen activator (tPA), urokinase, or streptokinase are not recommended as methods to reduce the need for shunt placement in premature infants with PHH. Strength of Recommendation: Level I, high clinical certainty.

Recommendation: Acetazolamide and furosemide are not recommended as methods to reduce the need for shunt placement in premature infants with PHH. Strength of Recommendation: Level I, high clinical certainty.

Timing of Shunt Placement

Recommendation: There is insufficient evidence to recommend a specific weight or CSF parameter to direct the timing of shunt placement in premature infants with PHH. Clinical judgment is required. Strength of Recommendation: Level III, unclear clinical certainty.

Endoscopic Third Ventriculostomy

Recommendation: There is insufficient evidence to recommend the use of endoscopic third ventriculostomy (ETV) in premature infants with PHH. Strength of Recommendation: Level III, unclear clinical certainty.

Acknowledgments

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Author contributions to the study and manuscript preparation include the following. Conception and design: AANS/CNS Joint Section on Pediatrics. Acquisition of data: all authors. Analysis and interpretation of data: all authors. Drafting the article: Mazzola. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Flannery. Administrative/technical/material support: all authors. Study supervision: Flannery.

References


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   tions of ventricular reservoirs in the treatment of post-haem-
   orrhagic ventricular dilatation: a retrospective study (1992-

   Gavilanes DA: Subcutaneous ventricular catheter reservoir and 
   ventriculoperitoneal drain-related infections in preterm infants 

   and hydrocephalus in premature newborns: a prospective study 

14. Chaparro MJ, Priz MB, Yonemura KS: Brovic ventriculotom-
   y for long-term external ventricular drainage. Pediatr 
   Neurosurg 17:208–212, 1992

15. Chaplin ER, Goldstein GW, Myerberg DZ, Hunt JV, Tooley 
   WH: Posthemorrhagic hydrocephalus in the preterm infant. 
   Pediatrics 65:901–909, 1980

16. Choudhary AR: Infantile hydrocephalus: management using 

17. Cornips E, Van Calenbergh F, Plets C, Devlieger H, Caspar E: 
   Use of external drainage for posthemorrhagic hydrocephalus 
   in very low birth weight premature infants. Childs Nerv 

18. de Vries LS, Liem KD, van Dijk K, Smit BJ, Ste I, Rademaker 
   KJ, et al: Early versus late treatment of posthaemorrhagic ven-
   tricular dilatation: results of a retrospective study from five 
   neonatal intensive care units in The Netherlands. Acta Paediatr 
   91:212–217, 2002

19. Dykes FD, Dunbar B, Lazarro A, Ahmann PA: Posthemor-
   rhagic hydrocephalus in high-risk preterm infants: natural 
   history, management, and long-term outcome. J Pediatr 114: 
   611–618, 1989

20. Elgamal EA, El-Dawlatly AA, Murshid WR, El-Watidy SM, 
   Jamjoom ZA: Endoscopic third ventriculostomy for hydro-
  cephalus in children younger than 1 year of age. Childs Nerv 

21. Felderhoff-Mueser U, Buhrer C, Groneck P, Obladen M, Bart-
   mann A, Herlein A, Soluble Fas (CD95/Apo-1), soluble Fas ligand, 
   and activated caspase 3 in the cerebrospinal fluid of infants 
   with posthemorrhagic and nonhemorrhagic hydrocephalus. 

22. Ferrell E, Hagberg G, Hagberg B: Infantile hydrocephalus in 
   preterm, low-birth-weight infants—a nationwide Swedish co-

23. Flammery AM, Mitchell L: Pediatric hydrocephalus: systematic 
   literature review and evidence-based guidelines. Part 1: Intro-
   3–7, 2014

24. Fulkerson AJ, Groenendaal F, van Stroo DW, Edwards JR, 
   Shoch MM, Boaz JC, et al: Progression of cerebrospinal fluid 
   cell count and differential over a treatment course of shunt infec-

25. Gaskill SJ, Marlin AE, Rivera S: The subcutaneous ventricu-
   lar reservoir: an effective treatment for posthemorrhagic hy-

26. Gurtner P, Bass T, Gudeman SK, Penix JO, Philput CB, 
   Schinco FP: Surgical management of posthemorrhagic hydro-
   cephalus in 22 low-birth-weight infants. Childs Nerv Syst 
   8:198–202, 1992

27. Haines SJ, Lapointe M: Fibrinolytic agents in the manage-
   ment of posthemorrhagic hydrocephalus in preterm infants: the 

28. Harbaugh RE, Saunders RL, Edwards WH: External ventricu-
   lar drainage for control of posthemorrhagic hydrocephalus in 

29. Heep A, Engelskirchen R, Holcschneider A, Groeneck P: Pri-
   mary intervention for posthemorrhagic hydrocephalus in very 
   low birthweight infants by ventriculostomy. Childs Nerv Syst 
   17:47–51, 2001

30. Horinek D, Cihar M, Tichy M: Current methods in the treat-
   ment of posthemorrhagic hydrocephalus in infants. Bratsil 

31. Hudgins RJ, Boydston WR, Gilreath CL: Treatment of post-
   hemorrhagic hydrocephalus in the preterm infant with a ven-

32. Hudgins RJ, Boydston WR, Hudgins PD, Morris R, Adler SM, 
   Gilreath CL: Intraventricular urokinase as a treatment for intra-
   ventricular hemorrhage in the preterm infant. Pediatr Neuro-
   surg 26:281–287, 1997

33. Inagaki T, Kawaguchi T, Yamahara T, Kitamura N, Ryu T, 
   Kinoshiya Y, et al: Management of intraventricular hemor-
   rhage in preterm infants with low birth weight. Acta Neuro-
   chir Suppl 113:173–175, 2012

34. International PHVD Drug Trial Group: International ran-
   domised controlled trial of acetazolamide and furosemide in 
   posthaemorrhagic ventricular dilatation in infancy. Lancet 

35. James HE: Spectrum of the syndrome of the isolated fourth 
   ventricle in posthemorrhagic hydrocephalus of the premature 

36. Kazan S, Gür A, Ucar T, Korkmaz E, Ongun H, Akyuz M: 
   Hydrocephalus after intraventricular hemorrhage in preterm 
   and low birth weight infants: analysis of associated risk fac-
   tors for ventriculoperitoneal shunting. Surg Neurol 64 Suppl 
   2:S77–S81, 2005

37. Kennedy CR, Ayers S, Campbell MJ, Elbourne D, Hope P, 
   Johnson A: Randomized, controlled trial of acetazolamide and 
   furosemide in posthaemorrhagic ventricular dilatation in in-

38. Korinth MC, Weinzierl MR, Glisbach JM: Experience with a 
   new concept to lower non-infectious complications in infants 

   of ventricular reservoir in preterm infants with post-hemor-
   rhagic ventricular dilatation does not increase the risk of res-
   ervor infection. J Perinatol 30:188–221, 2010

   progressive posthemorrhagic hydrocephalus. Treatment with 

41. Lam HP, Heilman CB: Ventricular access device versus ven-
   triculosubgaleal shunt in post hemorrhagocphalus associated 

42. Limbrick DD Jr, Baird LC, Klimo P Jr, Riva-Cambrin J, Flan-
   nery AM: Pediatric hydrocephalus: systematic literature re-
   view and evidence-based guidelines. Part 4: Cerebrospinal 
   fluid shunt or endoscopic third ventriculostomy for the treat-
   ment of hydrocephalus in children. J Neurosurg Pediatr 14 
   (Suppl):30–34, 2014

43. Limbrick DD Jr, Mathur A, Johnston JM, Munro R, Sagard A, 
   Inder T, et al: Neurosurgical treatment of progressive post-
   hemorrhagic ventricular dilatation in preterm infants: a 10-year 
   6:224–230, 2010

44. Lipina R, Reguli S, Dolezilová V, Kuncíková M, Podesvová 
   V, Cizek V, Clavé EM, Vagovicová J, Polidori G: Failure of fibrinolytic endoventricular treat-

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