

Pediatric hydrocephalus: systematic literature review and evidence-based guidelines. Part 8: Management of cerebrospinal fluid shunt infection

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Object. The objective of this systematic review was to answer the following question: What is the optimal treatment strategy for CSF shunt infection in pediatric patients with hydrocephalus?

Methods. The US National Library of Medicine and the Cochrane Database of Systematic Reviews were queried using MeSH headings and key words relevant to the objective of this systematic review. Abstracts were reviewed, after which studies meeting the inclusion criteria were selected and graded according to their quality of evidence (Classes I–III). Evidentiary tables were constructed that summarized pertinent study results, and based on the quality of the literature, recommendations were made (Levels I–III).

Results. A review and critical appraisal of 27 studies that met the inclusion criteria allowed for a recommendation for supplementation of antibiotic treatment using partial (externalization) or complete shunt hardware removal, with a moderate degree of clinical certainty. However, a recommendation regarding whether complete shunt removal is favored over partial shunt removal (that is, externalization) could not be made owing to severe methodological deficiencies in the existing literature. There is insufficient evidence to recommend the use of intrathecal antibiotic therapy as an adjunct to systemic antibiotic therapy in the management of routine CSF shunt infections. This also holds true for other clinical scenarios such as when an infected CSF shunt cannot be completely removed, when a shunt must be removed and immediately replaced in the face of ongoing CSF infection, or when the setting is ventricular shunt infection caused by specific organisms (for example, gram-negative bacteria).

Conclusions. Supplementation of antibiotic treatment with partial (externalization) or complete shunt hardware removal are options in the management of CSF shunt infection. There is insufficient evidence to recommend either shunt externalization or complete shunt removal as the preferred surgical strategy for the management of CSF shunt infection. Therefore, clinical judgment is required. In addition, there is insufficient evidence to recommend the combination of intrathecal and systemic antibiotics for patients with CSF shunt infection when the infected shunt hardware cannot be fully removed, when the shunt must be removed and immediately replaced, or when the CSF shunt infection is caused by specific organisms. The potential neurotoxicity of intrathecal antibiotic therapy may limit its routine use.

RECOMMENDATION: Supplementation of antibiotic treatment with partial (externalization) or with complete shunt hardware removal is an option in the management of CSF shunt infection. **STRENGTH OF RECOMMENDATION:** Level II, moderate degree of clinical certainty.

RECOMMENDATION: There is insufficient evidence to recommend either shunt externalization or complete shunt removal as a preferred surgical strategy for the management of CSF shunt infection. Therefore, clinical judgment is required. **STRENGTH OF RECOMMENDATION:** Level III, unclear degree of clinical certainty.

RECOMMENDATION: There is insufficient evidence to recommend the combination of intrathecal and systemic antibiotics for patients with CSF shunt infection in whom the infected shunt hardware cannot be fully removed or must be removed and immediately replaced, or when the CSF shunt infection is caused by specific organisms. The potential neurotoxicity of intrathecal antibiotic therapy may limit its routine use. **STRENGTH OF RECOMMENDATION:** Level III, unclear degree of clinical certainty.

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Key Words • cerebrospinal fluid shunt • infection • therapy • pediatrics • evidence-based guidelines • practice guidelines • hydrocephalus

CEREBROSPINAL fluid shunt infection is one of the most common and serious complications of CSF shunt therapy. Infection admissions number ap-

proximately 2300 per year in the United States and, in aggregate, account for more than 50,000 hospital days.²⁹ Total hospital charges related to the management of CSF shunt infection were nearly \$250 million in 2003 adjusted dollars.²⁹

Within 24 months after insertion, infections complicate approximately 11% of initial CSF shunt placements.²⁸

Abbreviations used in this paper: EVD = external ventricular drain; VA = ventriculoatrial; VP = ventriculoperitoneal.

Part 8: Management of CSF shunt infection

Despite the high incidence of this complication, the optimal management of CSF shunt infection has yet to be defined. The existing evidence regarding the management of CSF shunt infection is of poor methodological quality. As such, current management is dictated not by evidence, but rather by physician preference and other possibly relevant patient-level factors (for example, patient surgical risk, ventricle size, and complexity of the shunt system). It is not surprising that there is significant variation in CSF shunt infection treatment protocols between centers.³⁵

The objective of this systematic review was to answer the following question: What is the optimal treatment strategy for CSF shunt infection in pediatric patients with hydrocephalus? The successful treatment of CSF shunt infection aims to cure the infection (that is, minimize the probability of reinfection or relapse) while maintaining functional CSF diversion and minimizing morbidity, mortality, and the cost of therapy. The alternative paradigms for the management of ventricular shunt infection are illustrated well if one considers important historical milestones in the treatment of hydrocephalus. The evidentiary tables are structured somewhat accordingly (Fig. 1). The development of the Holter-Pudenz valve in 1957 and the ability to insert the distal end of a ventricular shunt into the right atrium was a major development in the treatment of hydrocephalus. Although ventriculoatrial (VA) shunts facilitated continuous and regulated CSF diversion, the fact that the distal catheter entered the heart posed logistical problems when these shunts inevitably became infected. A major issue with VA shunts was loss of limited venous access if these shunts were removed and not immediately replaced. In light of this limitation, the predominance of literature examining the treatment of CSF shunt infections in the era of VA shunts documented the outcomes of treatment with systemic antibiotics alone (Table 1) and whether the elevated CSF antibiotic concentrations achieved by intrathecal therapy conferred any additional benefit in managing the ventriculitis that often accompanied CSF shunt infection—both while leaving

the infected shunt in situ or after removing the shunt and immediately replacing it in infected cerebrospinal fluid (Table 2).

A decade later, Ames developed a technique for placement of the distal catheter in the peritoneal space, and as such, made shunt removal and later replacement a feasible surgical strategy in the management of CSF shunt infection. Over time, the combined medical and surgical treatment of ventricular shunt infection became more accepted, in part because of the gradual phase-out of VA shunts and their associated limitations with respect to repeated surgical access to the heart, but perhaps more significantly because of the realization that an infected ventricular shunt, as an infected foreign body, was difficult if not impossible to sterilize using antibiotics alone. This management philosophy accepts not only that shunt removal (and eventual replacement once CSF sterility is achieved) requires multiple surgeries, but also the risk of introducing secondary infection during a variable period of external drainage. Therefore, although more contemporary literature examining the treatment of CSF shunt infection consists of studies that incorporate some form of shunt removal, variations in whether the infected shunt was partially removed (that is, externalized) (Table 3) or completely removed (see Table 4), and whether supplemental intrathecal antibiotics were administered contribute to significant between-study heterogeneity.

A lack of rigorous comparative effectiveness studies leads to uncertainty regarding the preferred therapeutic strategy for a particular clinical circumstance. Decision analytical modeling attempts to apply statistical simulation techniques to preexisting data to rank competing therapeutic options in terms of their relative effectiveness. A decision analysis examining the treatment of CSF shunt infection using data from published studies (most included in evidentiary Tables 1–4) came to the conclusion that the best treatment modality for CSF shunt infection was antibiotic administration (systemic, with or without intrathecal administration) and complete removal

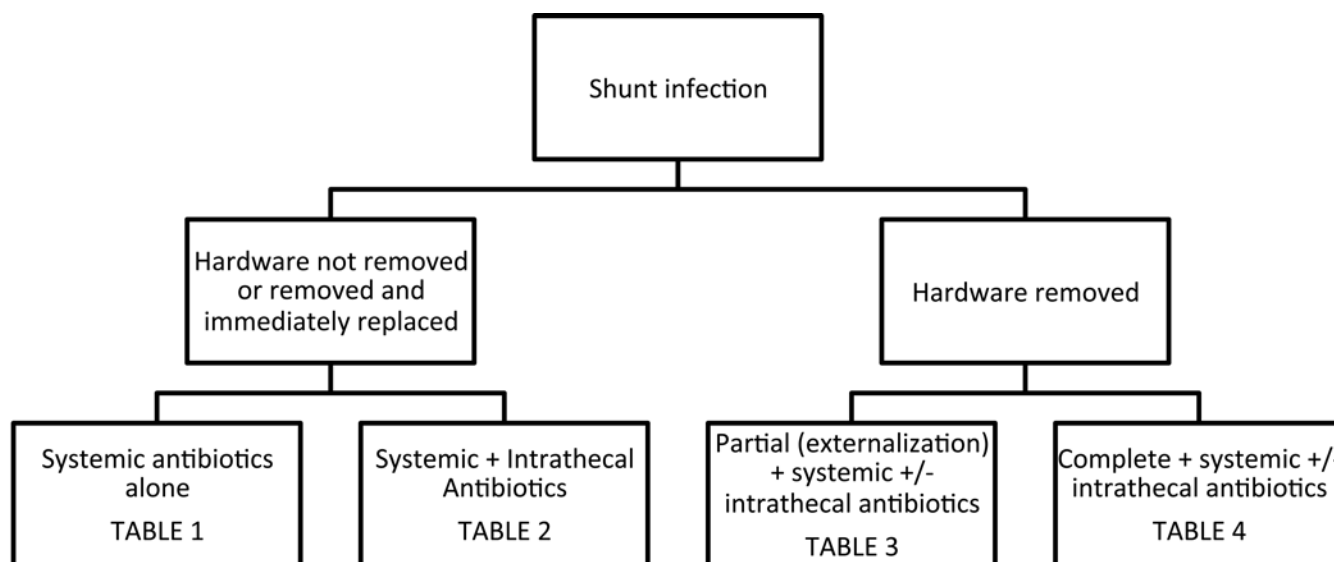


Fig. 1. Organization of evidentiary tables based on alternative paradigms for the management of CSF shunt infection.

TABLE 1: Systemic antibiotic treatment with shunt left in situ or removed and immediately replaced: summary of evidence*

Authors & Year	Study Description	Data Class, Quality, & Reasons	Results & Conclusions
Forrest et al., 1987	12 VA shunt infections w/ positive blood cultures (but sterile CSF) treated w/ IV antibiotics & complete shunt removal w/ immediate shunt replacement. Outcome: no evidence of recolonization at last follow-up (3–16 yrs).	Class III Retrospective case series. 11 other pts w/ positive blood & CSF cultures were treated w/ IV antibiotics, shunt removal, & EVD w/ delayed shunt replacement, but treatment outcomes are not presented.	12 of 12 pts w/ positive blood cultures but sterile CSF were w/o evidence of recolonization at last follow-up. Difficult to interpret findings in isolation.
Odio et al., 1984	59 shunt infections managed w/ systemic antibiotics alone (Group A, n = 13); systemic antibiotics + immediate shunt removal (Group B, n = 37); or systemic antibiotics + delayed shunt removal (Group C, n = 9). Outcome: cure (absence of shunt reinfection or relapse).	Class III Retrospective case series. Poor control of confounders. Reasons for immediate vs delayed shunt removal not given (selection bias). Timing of outcome assessment not given.	Cure in 8 of 13 pts treated w/ antibiotics alone, 34 of 37 pts treated w/ antibiotics + immediate shunt removal, & 8 of 9 pts w/ antibiotics + delayed shunt removal. Results suggest a poorer outcome w/o shunt removal.
Walters et al., 1984	267 infections treated in 222 pts. 92 treated medically (85 systemic, 7 systemic + IT antibiotics); 117 treated medically + surgically (21 pts: the shunt was removed & immediately replaced under antibiotic coverage; 51 pts: shunt removal + antibiotics + delayed shunt replacement; 20 pts: shunt removal + EVD/shunt externalization + IT antibiotics; 25 pts: shunt removal + antibiotics w/o shunt replacement); 58 pts: no specific treatment of shunt infection (e.g., unrecognized shunt infection). Outcome: death.	Class III Retrospective case series. Definition of cure (another tabulated outcome) not provided. Multiple different permutations & combinations of treatment w/o clear criteria matching a particular patient w/ a particular treatment (selection bias). Nontraditional outcome.	37% mortality w/ medical management alone. 18% mortality w/ medical + surgical therapy; lowest mortality in those in whom shunt was removed & replaced under antibiotic coverage in a single operation. Addition of surgical therapy appears to lower morbidity & mortality of shunt infection.
Schoenbaum et al., 1975	98 shunt infections among 442 shunt procedures in 289 pts. Initial treatment based on shunt type. VP shunts were all completely removed & treated w/ IV antibiotics; some pts w/ VA & V-ureteral shunts were initially managed w/ IV antibiotics alone. Outcome: death.	Class III Retrospective case series. Poor control of confounders. Selection bias. Authors cite “control of infection” as outcome, but not clearly defined. Nontraditional outcome.	1 of 30 pts treated w/ complete shunt removal & IV antibiotics died; 28 of 30 pts obtained control of infection. 6 of 43 pts w/ VA & V-ureteral shunts treated w/ IV antibiotics alone died; 13 of 43 pts obtained control of infection. Shunt removal is required for improved outcome.
Shurtleff et al., 1974	67 pts w/ shunt infection treated w/ IV antibiotics alone (Group A, n = 22); IV antibiotics + shunt revision (Group B, n = 14); IV antibiotics + complete shunt removal & replacement (Group C, n = 12); IV + IT antibiotics + complete shunt removal & replacement (Group D, n = 7); IV + IT/intrashunt antibiotics alone (Group E, n = 10); or IV + IT antibiotics w/ shunt revision (Group F, n = 2). Outcome: cure (no symptoms & at least 6 negative blood cultures & 2 negative ventricular/shunt CSF cultures during a 6-mo period after cessation of antibiotics).	Class III Retrospective case series. No control of confounders. Rationale for selecting different therapies for different infections not clear (“therapy evolved during the study”) (selection bias).	Cure in 2 of 22 pts (Group A), 3 of 14 pts (Group B), 12 of 12 pts (Group C), 7 of 7 pts (Group D), 3 of 10 pts (Group E), & 0 of 2 pts (Group F). Highest cure rate in pts w/ complete shunt removal & replacement, irrespective of whether they received supplemental IT antibiotics.

(continued)

TABLE 1: Systemic antibiotic treatment with shunt left in situ or removed and immediately replaced: summary of evidence* (continued)

Authors & Year	Study Description	Data Class, Quality, & Reasons	Results & Conclusions
Morrice & Young, 1974	Pts w/ colonization of VA shunt valves treated w/ antibiotics alone (n = 14); removal & immediate replacement of shunt (n = 23); or removal of shunt w/ a period of external drainage, followed by delayed shunt insertion (n = 19). Outcome = "alive & well" at 6 mos.	Class III Retrospective case series. Poor control of confounders. Selection bias. Route of administration of antibiotics not specified. Unclear if pts who underwent surgical treatment (immediate or delayed shunt replacement) received supplemental antibiotics. No specific microbiological component of outcome.	2 of 14 pts treated w/ antibiotics alone are alive & well at 6 mos. 11 of 23 pts treated w/ removal & immediate replacement of shunt are alive & well at 6 mos. 8 of 19 pts treated w/ removal of shunt w/ a period of external drainage, followed by delayed shunt insertion are alive & well at 6 mos. Results suggest that shunt removal is required to optimize outcome.
Nicholas et al., 1970	60 infections of VA shunts treated w/ IV antibiotics (also IT antibiotics if the CSF was infected) & delayed shunt replacement (n = 33 infections) or w/ IV antibiotics & immediate shunt replacement (n = 27 infections). Outcome: "Subsequent good health of the patient & freedom from bacteremia."	Class III Retrospective case series. No control of confounders. Selection bias. Nondescript outcome.	Successful treatment in 24 of 33 infections treated w/ IV antibiotics (also IT antibiotics if the CSF was infected) & delayed shunt replacement vs 21 of 27 infections treated w/ IV antibiotics & immediate shunt replacement. Recurrence/relapse higher in pts w/ immediate shunt replacement.

* IT = intrathecal; IV = intravenous; pts = patients; V-ureteral = ventriculoureteral.

of the infected shunt, with intercurrent external ventricular drainage or ventricular taps, followed by placement of a new shunt when CSF sterility is achieved. Sensitivity analyses revealed that this treatment option had the highest cure rate, the lowest failure rate, and the lowest mortality rate when compared with treatment consisting of antibiotic therapy with shunt removal and immediate replacement, or antibiotic treatment alone, over a wide range of assumptions.²³

Multiple review articles on the topic also conclude that shunt infection should be ideally managed with antibiotics, complete shunt removal, and placement of a temporary external ventricular drain (EVD), followed by reimplantation after CSF sterilization.^{1,4,7,36,37} Although intrathecal administration of antibiotics appears to make theoretical sense because of enhanced CSF antibiotic concentrations, its practical application is controversial, owing in large part to the potential adverse effects of intrathecal therapy, including neurotoxicity. The indications for intrathecal therapy are not well established and presently range from use in any shunt infection, use in only those infections in which the CSF cannot be sterilized by systemic antibiotics alone (for example, persistent positive cultures), or use in those ventricular shunt infections caused by specific organisms (for example, gram-negative infections).

A practice survey of board-certified members of the American Society of Pediatric Neurosurgeons revealed that most surgeons treat ventricular shunt infection with antibiotics, removal of the infected CSF shunt, and placement of an EVD, followed by delayed shunt replacement—a management paradigm that can be supported by the available evidence, as detailed below.³⁵

Methods

Search Criteria

We searched the US National Library of Medicine (PubMed/MEDLINE) database and the Cochrane Database of Systematic Reviews for the period January 1966 through March 2012 using the following MeSH subject headings: (CSF shunts) AND (bacterial infection OR prosthesis-related infection OR catheter-related infection) AND (treatment OR outcome) AND (antibacterial agents OR injections OR antibiotics OR device removal OR ventriculostomy OR combined modality therapy). Searches were limited to studies in patients younger than 18 years of age, the management of initial (not repeat) CSF shunt infection, and to the English language.

Search Results

A total of 342 abstracts were screened and 69 full-text articles were retrieved for review. The details of this process are described in Part 1, the introduction and methodology section of these guidelines.⁵ An examination of the reference lists of these 69 full-text articles yielded an additional 24 articles that warranted full-text review (Fig. 2). Subsequent review of the full texts of these 93 articles led to the exclusion of 66 articles based on predefined criteria, leaving 27 articles as the basis for

TABLE 2: Systemic and intrathecal antibiotic treatment with shunt left in situ or removed and immediately replaced: summary of evidence*

Authors & Year	Study Description	Data Class, Quality, & Reasons	Results & Conclusions
James et al., 1981	50 pts (30 reported in James et al., 1980 RCT) w/ shunt infection treated w/ shunt removal, systemic antibiotics, & either EVD or ventricular taps for decompression & antibiotic administration (Group A, n = 22); removal & immediate replacement of shunt w/ intrashunt & systemic antibiotics (Group B, n = 17); or intrashunt & systemic antibiotics w/o shunt removal (Group C, n = 11). Outcome: negative ventricular CSF cultures 48 hrs after cessation of antibiotic therapy & again w/in 4 mos of completion of therapy.	Class II Prospective nonrandomized cohort. Continuation of James et al., 1980 RCT—high incidence of failures in medical management arm (i.e., no shunt removal) made further randomization unjustified.	21 of 22 pts in Group A were successfully treated. 15 of 17 pts in Group B were successfully treated. 4 of 11 pts in Group C were successfully treated. Suggests better treatment outcomes w/ shunt removal. Suggests that IT antibiotics may be of use if shunt must be removed & immediately replaced rather than replaced in a delayed fashion (when infection has been cleared).
James et al., 1980	30 pts w/ shunt infection treated w/ shunt removal, systemic antibiotics, & either EVD or ventricular taps for decompression & antibiotic administration (Group A, n = 10); removal & immediate replacement of shunt w/ intrashunt & systemic antibiotics (Group B, n = 10); or intrashunt & systemic antibiotics w/o shunt removal (Group C, n = 10). Outcome: negative ventricular CSF cultures 48 hrs after cessation of antibiotic therapy & again w/in 4 mos of completion of therapy.	Class II RCT w/ design flaws. Suboptimal randomization & allocation. Baseline characteristics of treatment groups not documented. Unclear if outcome assessment was blinded. Underpowered (but study terminated early for harm).	10 of 10 pts in Group A were successfully treated. 9 of 10 pts in Group B were successfully treated. 3 of 10 pts in Group C were successfully treated. Length of hospital stay lowest in Group A. Deaths only occurred in Group C. Suggests better treatment outcomes w/ shunt removal. Suggests that IT antibiotics may be of use if shunt must be removed & immediately replaced rather than replaced in a delayed fashion (when infection has been cleared).
Bayston & Rickwood, 1981	43 children w/ staphylococcal VA or VP shunt infection treated w/ antibiotics alone (systemic or systemic + IT). Outcome: eradication of infection (response during treatment w/ no clinical relapse, followed by repeated normal serological & bacteriological studies).	Class III Retrospective case series. Timing of outcome assessment not clear.	Eradication of infection in 5 of 43 pts. 4 of 5 of those pts w/ eradication of infection received IT antibiotics. No eradication of <i>Staphylococcus aureus</i> shunt infection. Suggests the utility of supplemental IT antibiotics if the shunt cannot be removed.
Wald & McLaurin, 1980	20 pts w/ shunt infection treated w/ daily IT antibiotics (w/ systemic antibiotics) w/o removal of the shunt or EVD placement. Outcome: cure (2 or 3 sterile CSF cultures 72 hrs after completion of antibiotics).	Class III Retrospective case series. Pharmacodynamic study.	"Cure" in 5 of 7 pts receiving at least 7 days of IT methicillin. "Cure" in 4 of 5 pts treated w/ IT gentamicin. "Cure" in 6 of 7 pts receiving a single 2-wk course of IT cephalothin. Rates of "cure" appear higher than medically treated pts receiving systemic antibiotics alone.
Sells et al., 1977	20 gram-negative shunt infections receiving 25 total treatment trials. Treatments were none (n = 2); systemic antibiotics alone (n = 4); systemic & intraventricular antibiotics alone (n = 4); systemic antibiotics plus in situ shunt replacement (i.e., into the infected tract or incomplete shunt replacement (n = 2); systemic & intraventricular antibiotics w/ in situ shunt replacement (i.e., into the infected tract) or incomplete shunt replacement (n = 4); systemic & intraventricular antibiotics w/ complete shunt removal or replacement in a new site (n = 9). Outcome: cure (asymptomatic patient w/ at least 6 negative blood cultures & 2 negative ventricular or shunt CSF cultures obtained during a 6-mo period after cessation of antibiotics).	Class III Retrospective case series. Poor control of confounders. Selection bias. Very few pts receiving each individual treatment.	Cure in 0 of 2 pts receiving no treatment. Cure in 1 of 4 pts receiving systemic antibiotics alone. Cure in 0 of 4 pts receiving systemic & intraventricular antibiotics alone. Cure in 1 of 2 pts receiving systemic antibiotics plus in situ shunt replacement or incomplete shunt replacement. Cure in 0 of 4 pts receiving systemic & intraventricular antibiotics w/ in situ shunt replacement or incomplete shunt replacement. Cure in 9 of 9 pts receiving systemic & intraventricular antibiotics w/ complete shunt removal or replacement in a new site. Clear advantage of complete vs incomplete shunt removal. No clear additional advantage of IT antibiotics in pts treated medically or medically w/ in situ shunt replacement or incomplete shunt replacement.

(continued)

TABLE 2: Systemic and intrathecal antibiotic treatment with shunt left in situ or removed and immediately replaced: summary of evidence* (continued)

Authors & Year	Study Description	Data Class, Quality, & Reasons	Results & Conclusions
McLaurin, 1975	25 shunt infections (23 VA & 2 VP) treated w/ IV + IT antibiotics & delayed shunt replacement (n = 4), IV + IT antibiotics w/ immediate shunt replacement (n = 10), or IV + IT antibiotics alone (n = 11). Outcome: absence of residual infection at last follow-up (6 mos–5 yr).	Class III Retrospective case series. Characteristics of those pts successfully treated w/ IV + IT antibiotics alone (i.e., w/o shunt removal & replacement) not documented (selection bias). Extension of McLaurin, 1975 series.	Absence of residual infection at last follow-up in all 24 surviving pts (infection believed to have been cured in the 1 patient who died). Suggests that IT antibiotics may be of use if shunt is not removed or must be removed & immediately replaced. Shunt removal may not be necessary for successful treatment of shunt infection if IT antibiotics are administered.

* RCT = randomized controlled trial.

the evidentiary tables for this particular recommendation. Reasons for exclusion of full-text articles included the following: literature review (n = 19); no treatment outcomes given (n = 14); pediatric patients not reported separately (n = 6); wrong target population (n = 1); small sample size (n = 19); not a full report of a clinical study (n = 2); not relevant to the study question (n = 3); and other (n = 2).

Results

In general, the methodological quality of the evidence related to this recommendation was poor. The studies that met our inclusion criteria were typically descriptive series of small numbers of patients and were vulnerable to the biases and limitations of a retrospective study design. Because the studies relied on the accuracy and completeness of the medical record, the control of potentially confounding variables was nonexistent. Although most studies did compare outcomes between patient groups treated under alternative management protocols, the rationale behind why a particular treatment was assigned to a particular patient group was not clearly described, leading to significant issues with selection bias. For those studies describing the outcomes of a single management protocol, between-study comparisons of results was hampered by widely disparate management protocols and the use of nonuniform outcome measures (and definitions thereof). These limitations precluded, for the most part, any meaningful quantitative synthesis of the data; what follows is a largely qualitative review of the evidence relevant to this recommendation.

Despite the overall predominance of Class III data, the 13 studies presented in evidentiary Tables 1^{6,17–19,22,27,33} and 2^{3,11,12,16,25,32} are quite suggestive of the notion that in the management of CSF shunt infection, supplementation of antibiotic treatment with partial (externalization) or complete shunt hardware removal should be considered. Two Class II studies provide particularly compelling evidence in favor of a combined medical and surgical management of CSF shunt infection, and deserve to be elaborated on further.

In 1980, James et al.¹² published the results of a moderate-quality randomized controlled trial in which 10 patients with evidence of CSF shunt infection were randomized to each of 3 different treatment arms: 1) complete shunt removal, systemic antibiotics, and either external ventricular drainage or ventricular taps for decompression and intrathecal antibiotic administration, with delayed shunt replacement; 2) complete shunt removal and immediate shunt replacement with intrashunt and systemic antibiotics; or 3) intrashunt and systemic antibiotics without shunt removal. The outcome was negative ventricular CSF cultures 48 hours after cessation of antibiotic therapy and again within 4 months of completion of therapy. All 10 patients who underwent complete shunt removal, systemic antibiotics, and either external ventricular drainage or ventricular taps for decompression and intrathecal antibiotic administration were successfully treated. Nine of 10 patients treated with complete shunt removal and immediate shunt replacement with intrashunt and systemic antibiotics achieved therapeutic success. In con-

TABLE 3: Partial shunt removal and treatment with systemic antibiotics or with systemic and intrathecal antibiotics: summary of evidence

Authors & Year	Study Description	Data Class, Quality, & Reasons	Results & Conclusions
James & Bradley, 2008 ¹⁰	Prospective nonrandomized study of 2 protocols for treating complicated shunt infections (multiloculated, multiorganism, infection at other site in body). Group A, n = 21 treated w/ IV (2 wks) & IT antibiotics injected through EVD (n = 10) or reservoir of externalized shunt (n = 11) (2×/wk for 2 wks). 3 wks of antibiotics in total. Outcome: cure (cultures 48 hrs after cessation of antibiotics, at time of new shunt placement, & 3–6 mos later remained negative). Group B, n = 18 treated w/ IV (2 wks) & IT antibiotics injected through EVD or reservoir of externalized shunt (1×/wk for 2 wks). 3 wks of antibiotics in total. Outcome: cure (cultures 24 hrs after cessation of antibiotics, at time of new shunt placement, & 3–6 mos later remained negative).	Class III Nonrandomized, prospective case series. Outcome is different for each treatment group.	All pts treated according to either protocol were cured. Length of stay protocol in Group A = 25.1 days vs protocol in Group B = 19.7 days. No recurrent shunt infections during the follow-up period. Pts w/ complicated shunt infections can be successfully treated w/ 2 wks of once daily IT therapy concurrent w/ 3 wks of IV therapy (& EVD or shunt externalization).
Arnell et al., 2007	Retrospective review of 34 consecutively treated intraventricular shunt infections treated w/ externalization of the ventricular catheter proximal to the valve, daily IT injections (generally guided by CSF antibiotic concentrations, median 8 days), & IV antibiotics (median 10 days). Usually no antibiotics after shunt replacement. Outcome: cure (sterilization of CSF & resolution of clinical symptoms).	Class III Retrospective case series. No control of confounders.	CSF sterilized in 1 of 3, 7 of 8, 20 of 20, & 6 of 6 cases after 1, 2, 3, & >3 days of therapy (externalization of ventricular catheter & start of IT antibiotics). Clinical symptoms resolved in parallel w/ the sterilization of CSF. Despite the ventricular catheter being left in place & the short duration of therapy, the treatment protocol results in quick CSF sterilization, a low relapse rate, & survival of all pts in this series.
Wang et al., 1999	23 pts treated according to a documented management protocol (externalization of distal catheter unless failure to sterilize CSF, empiric followed by tailored antibiotics for 10 days following sterilization of CSF, reimplantation of shunt if cultures remain negative for 3 days off antibiotics). Comparison group of 10 historical controls treated w/ an undisclosed regimen. Outcome: recurrence (reinfection w/ same organism w/in 6 mos).	Class III Comparative study w/ historical controls. No control of confounders. 3 pts had a ventricular reservoir only. Details of treatment of historical control pts not clear (“duration of antibiotic therapy for each individual case was decided arbitrarily”).	Reinfection 0 of 15 pts treated under protocol (8 pts did not require shunt reinsection) vs 2 of 10 treated before protocol. Shorter hospital stay in those treated under the protocol. Of those treated under the protocol, pts w/ a “complex” shunt system required longer hospitalization. This treatment protocol may be effective in the management of shunt infection.
Ronan et al., 1995	41 episodes of infection in 39 children treated w/ antibiotics (28 IV & oral, 11 IV + IT + oral, 4 IT + IV, 1 IT + oral) & surgical treatment (complete or partial shunt removal & immediate or delayed replacement w/ or w/o external ventricular drainage). Outcome: absence of relapse (reinfection w/ same organism) at 3 mos, & was verified by the absence of relapse for the follow-up period (min 1 year).	Class III Retrospective case series. Selection bias. Overall management approach too varied to allow for reasonable conclusions to be made.	Absence of relapse in 31 pts, relapse in 6 pts, death in 4 pts (not directly related to shunt infection). Outcome not dependent on length of antibiotic treatment or use of IT antibiotics. Surgical approach to treatment too varied to permit conclusions about efficacy. Complete shunt replacement associated w/ lower risk of relapse vs partial replacement, & delayed replacement had better outcomes vs immediate replacement.

trast, only 3 of 10 patients who received systemic and intrathecal antibiotics without shunt removal were successfully treated. The treatment results in this latter group rather clearly demonstrate that shunt removal, rather than antibiotic therapy (including intrathecal therapy), was

responsible for the improved outcomes seen in the comparison groups. Secondary outcomes also were consistent with a benefit toward surgical removal of the shunt, as length of hospital stay was lowest in those patients who underwent complete shunt removal with delayed shunt re-

TABLE 4: Complete shunt removal and treatment with systemic or systemic and intrathecal antibiotics: summary of evidence

Authors & Year	Study Description	Data Class, Quality, & Reasons	Results & Conclusions
Kestle et al., 2006	70 pts from 10 centers followed prospectively for 1 yr following successful treatment of shunt infection. Initial management was shunt externalization & antibiotics in 17 pts; shunt removal, EVD insertion, & antibiotics in 50 pts; & antibiotic treatment alone in 3 pts. Outcome: culture-proven reinfection (same or different organism).	Class II Prospective multicenter observational study. Reinfection rates in those externalized vs completely removed not provided separately. Timing of outcome assessment not clear.	Reinfection occurred in 18 pts (26%); in 12 pts due to the same initial organism & in 6 pts due to different organisms. Reinfection risk was not associated w/ length of antibiotic treatment. This study reconfirms the high reinfection rate in pts receiving treatment for shunt infection.
Shimizu et al., 2012	Retrospective chart review of 36 pts w/ shunt removal, EVD placement (in 4 pts there was externalization prior to EVD placement), IV antibiotics, & eventual shunt replacement, compared to 9 pts w/ shunt removal, IV antibiotics, & ETV for treatment of shunt infection. Outcome: recurrence of CSF infection w/in 6 mos after shunt reinsertion or ETV.	Class III Retrospective case series. No control of confounders. Selection bias.	Of those treated w/ shunt removal followed by reinsertion, 10 of 36 experienced CSF reinfection. This study reconfirms the high reinfection rate in pts receiving treatment for shunt infection.
James & Bradley, 2008 ⁹	Retrospective nonrandomized comparison of 2 protocols for treating uncomplicated shunt infections (single shunt system, single organism, noncompartmentalized hydrocephalus). Group A, n = 25 w/ shunt removal/EVD, IV antibiotics until clinical course & CSF values suggested cure of infection, IT antibiotics 2x/wk through EVD or at times of ventricular puncture. Outcome: cure (cultures 48 hrs after cessation of antibiotics, at time of new shunt placement, & 3–6 mos later remained negative). Group B, n = 15 w/ shunt removal/EVD, IV antibiotics until clinical course & CSF values suggested cure of infection, IT antibiotics 1x/wk through EVD or at times of ventricular puncture. Outcome: cure (cultures 24 hrs after cessation of antibiotics, at time of new shunt placement, & 3–6 mos later remained negative).	Class III Retrospective comparative study. Outcome is different for each treatment group.	All pts treated according to either protocol were cured. Duration of IV antibiotics: Protocol A = 9.7 days vs Protocol B = 9.9 days. Pts w/ a single shunt infected w/ a single organism & w/ noncompartmentalized hydrocephalus may be successfully treated w/o a prolonged antibiotic course & lengthy hospital stay, provided the shunt is completely removed.
Schuhmann et al., 2005	35 consecutive culture-proven shunt infections were treated w/ antibiotics, surgery for shunt removal/EVD placement, or shunt externalization & eventual reinternalization of the shunt. Outcome: shunt reinfection.	Class III Prospective case series. Details of management of shunt infection not clear (e.g., no. of pts who underwent complete vs incomplete shunt removal & no. of pts who had intrathecal supplementation to systemic antibiotic therapy, if any). Outcomes not provided separately for shunts externalized vs shunts completely removed.	6 of 33 pts experienced a shunt reinfection. This study reconfirms the high reinfection rate in pts receiving treatment for shunt infection.
Turgut et al., 2005	37 infections in 35 pts. 31 pts treated w/ shunt removal, EVD, & systemic + IT antibiotics. 4 pts treated w/ medical management alone. Outcome: death.	Class III Retrospective case series. Nontraditional outcome. Criteria for treating 4 pts medically not clear (selection bias).	2 of 31 pts treated w/ shunt removal, EVD, & systemic + IT antibiotics died. 1 of 4 pts treated medically died. Good outcomes w/ IT therapy, but no pts underwent shunt removal w/ systemic antibiotics alone.

(continued)

TABLE 4: Complete shunt removal and treatment with systemic or systemic and intrathecal antibiotics: summary of evidence (*continued*)

Authors & Year	Study Description	Data Class, Quality, & Reasons	Results & Conclusions
Mancao et al., 1998	29 consecutive shunt infections treated. 27 pts had shunt removal ± external drainage. All received IV antibiotics, & 6 pts received supplemental IT antibiotics. Outcome: relapse of infection.	Class III Retrospective case series. Definition of outcome (relapse) not provided; follow-up period was not defined. Criteria for IT antibiotics not given.	27 pts had successful treatment (no relapse), 2 deaths not clearly related to shunt infection. This study demonstrates a lower rate of reinfection than other studies, but the data are of poor quality.
Stamos et al., 1993	23 consecutive gram-negative shunt infections, managed w/ complete shunt removal, EVD, & IV antibiotics (n = 19) or IT antibiotics (n = 2) for persistent positive cultures. Outcome: "cure" (asymptomatic & at least 3 negative cultures after cessation of antibiotics), after which shunt was reinserted.	Class III Retrospective case series. No control of confounders.	All pts obtained cure w/ shunt removal, EVD placement, & antibiotics (19 IV, 2 IV + IT). On late follow-up of 19 pts (>6 mos), 4 had subsequent coagulase-negative staphylococcal infection. Despite initial success, reinfection rates appear similarly high when compared w/ other studies.
Kontry et al., 1993	28 infections in 25 pts, treated w/ IV antibiotics & immediate removal of the shunt system (n = 24) or IV antibiotics alone (n = 4). Outcome: reinfection or relapse w/in 1 mo of completion of therapy.	Class III Retrospective case series. Details of management of infection not given. Short follow-up.	All pts were w/o reinfection or relapse. Short follow-up precludes definitive conclusions.
James et al., 1984	18 infections (13 following initial shunt procedure & 5 following revisions) in low-birth-weight infants (<2000 g) treated promptly w/ shunt removal & IV + IT antibiotics (see James et al., 1980). Outcome: cure.	Class III Retrospective case series. Outcome not clearly defined (although, if per James 1980, then as follows: Negative cultures 48 hrs after cessation of antibiotics & w/in 4 mos of completion of therapy).	All except 1 patient demonstrated cure when treated according to protocol. Good outcomes w/ IT therapy, but no pts underwent shunt removal w/ systemic antibiotics alone.
Scarff et al., 1978	57 children w/ shunt-related ventricular infection treated w/ IV + IT antibiotics & external ventricular drainage (either shunt removal & EVD, or shunt externalization). Outcome: clearance of infection (3 consecutive cultures w/ negative growth at 48 hrs).	Class III Retrospective case series. No. of pts receiving each surgical therapy (shunt removal & EVD, or shunt externalization) were not documented, nor were their outcomes differentially reported.	54 of 57 pts demonstrated clearance of infection. Good outcomes w/ IT therapy, but no pts underwent shunt removal w/ systemic antibiotics alone.

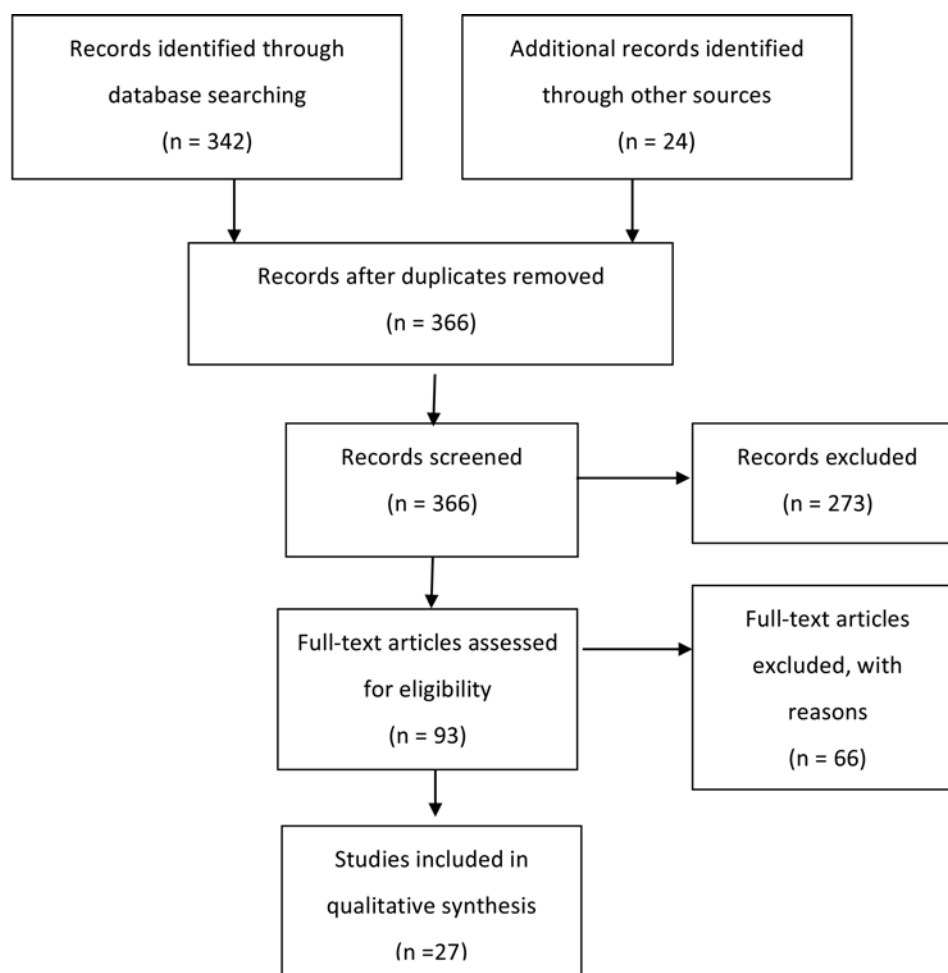


Fig. 2. Flowchart showing the process involved in identifying relevant literature.

placement after a course of systemic and intrathecal antibiotics. The only deaths occurred in those patients who received medical management alone. Because of the convincing inferiority of medical management alone, further randomization to this group was halted, but the study was continued as a prospective nonrandomized comparison of treatment outcomes between those patients receiving intrathecal and systemic antibiotics in conjunction with complete shunt removal and delayed versus immediate shunt replacement.¹¹ The principal conclusions remain unchanged.

The nearly equivalent treatment outcomes of shunt removal followed by immediate shunt replacement (that is, shunt replacement in infected CSF) versus delayed shunt replacement (that is, shunt replacement after the CSF has been sterilized) in the aforementioned studies by James and colleagues^{11,12} was suggestive of the potential utility of intrathecal antibiotics in those clinical circumstances in which the shunt must be removed and immediately replaced. As such, these studies provide some evidence applicable to the intrathecal antibiotic recommendation as well. As outlined earlier, it appears that most of the treatment effect comes from shunt removal, making the relative contribution of intrathecal antibiotics to improved outcomes in this scenario rather uncertain. Hence, elevat-

ing the recommendation for intrathecal antibiotics to a Level II recommendation, based on these relatively high quality data alone, appears unwarranted.

Additional evidence pertaining to the intrathecal antibiotic recommendation comes largely from Class III studies that examined the results of treatment of ventricular shunt infection in those clinical circumstances in which the infected shunt components are not removed (Table 2^{3,11,12,16,25,32}) or only partially removed (that is, externalized) (Table 3^{2,10,20,34}). There was a Class III study that documented a fairly large proportion of patients who achieved therapeutic success—comparable to the success seen in patients who underwent shunt removal—when the patients were treated with intrathecal antibiotics but their shunts were left in situ.¹⁶ In addition, Bayston and Rickwood³ documented eradication of staphylococcal VA or VP shunt infection in 5 of 43 patients who underwent antibiotic treatment alone; 4 of the 5 patients who were successfully treated received intrathecal antibiotics. In cases in which ventricular shunt infection was treated with systemic and intrathecal antibiotics along with shunt externalization, either because of the complexity of the shunt infection scenario (for example, multiloculated hydrocephalus) or surgeon preference, a prospective non-randomized study by James and Bradley¹⁰ and a Class III

study by Arnell et al.² were both able to demonstrate positive treatment outcomes in all patients in their respective case series. Finally, another retrospective case series by James and Bradley⁹ showed convincingly high cure rates with a significantly shorter length of stay in those patients with an uncomplicated shunt infection (that is, a single shunt system) treated with complete shunt removal together with systemic and intrathecal antibiotics (Table 4). Unfortunately, the absence of a concurrent control group treated with shunt removal and systemic antibiotics alone in this and other studies listed in Table 4 limits the impact of these data to the overall body of evidence.

When examining the studies presented in evidence in Table 3^{2,10,20,34} and Table 4,^{8,9,13–15,21,24,26,30,31} it is difficult to say with any degree of clinical certainty whether complete shunt removal leads to better shunt infection treatment outcomes than partial shunt removal. This is due, in part, to the paucity of outcome data comparing the 2 treatment options within the same study population, but also to the confounding effect of intrathecal antibiotic therapy, as described above.

After a full-text review of the contents of papers that were initially identified through our search strategy or our scrutiny of reference lists, predefined criteria led to the exclusion of multiple studies from the evidentiary tables. The recommendations provided above are not materially changed by the exclusion of these studies.

Conclusions

RECOMMENDATION: Supplementation of antibiotic treatment with partial (externalization) or with complete shunt hardware removal is an option in the management of CSF shunt infection. **STRENGTH OF RECOMMENDATION:** Level II, moderate degree of clinical certainty.

RECOMMENDATION: There is insufficient evidence to recommend either shunt externalization or complete shunt removal as a preferred surgical strategy for the management of CSF shunt infection. Therefore, clinical judgment is required. **STRENGTH OF RECOMMENDATION:** Level III, unclear degree of clinical certainty.

RECOMMENDATION: There is insufficient evidence to recommend the combination of intrathecal and systemic antibiotics for patients with CSF shunt infection in whom the infected shunt hardware cannot be fully removed or must be removed and immediately replaced, or when the CSF shunt infection is caused by specific organisms. The potential neurotoxicity of intrathecal antibiotic therapy may limit its routine use. **STRENGTH OF RECOMMENDATION:** Level III, unclear degree of clinical certainty.

It appears that the optimal management of CSF shunt infection requires a multimodality approach. Review and critical appraisal of the available evidence regarding the management of ventricular shunt infection allow for a recommendation for the supplementation of antibiotic treatment with partial (externalization) or complete shunt hardware removal with a moderate degree of clinical certainty. However, a recommendation regarding whether complete shunt removal is favored over partial shunt removal (that is, externalization) cannot be made, owing to severe methodological deficiencies in the exist-

ing literature. Furthermore, there is insufficient evidence to recommend the use of intrathecal antibiotic therapy as an adjunct to systemic antibiotic therapy in the management of routine CSF shunt infections, or in other clinical scenarios, such as when an infected CSF shunt cannot be completely removed, must be removed and immediately replaced in the face of ongoing CSF infection, or in the setting of ventricular shunt infection caused by specific organisms (for example, gram-negative bacteria).

Deficiencies in the existing literature regarding the management of CSF shunt infection provide a strong rationale for further prospective research into the subject. Key questions that remain unanswered include, but are certainly not limited to the following:

- Defining the optimal duration of antibiotic therapy in the management of CSF shunt infection, with the aim of simultaneously maximizing the probability of successful treatment without reinfection or relapse, and minimizing the length of hospital stay and overall cost to the health care system.
- Refining the indications for intrathecal antibiotic therapy and ascertaining the risk/benefit profile of such therapy (potential adverse effects vs potential reduction in relapse/reinfection rates and shorter hospital stays).
- Definition and validation of standardized treatment outcome measures, based on microbiological or other biomarker-based criteria. This would not only facilitate a comparison of results across studies, but also potentially yield objective criteria that facilitate decision making in other contentious areas of CSF shunt infection management, such as the optimal timing of shunt reimplantation.

Perhaps the best strategy to treat ventricular shunt infection is to continue our focus on the prevention of this significant complication of CSF shunt therapy.

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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.

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