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Treatment strategies for cerebrospinal shunt infections: a systematic review of observational studies

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ABSTRACT

Objective A systematic review was conducted of studies comparing time to cerebrospinal fluid (CSF) sterilisation or rate of recurrence with different treatment strategies for CSF shunt infections.

Methods A librarian-directed search was conducted of Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid Medline Daily and Ovid Medline, Ovid Embase, Wiley Cochrane Library, CINAHL Plus with Full Text via EBSCOhost, Scopus Advanced Search, and Web of Science Core Collection from 1990 to May 2019. Studies of any design that compared outcomes in groups of any age with different management strategies were included. Studies that compared complete versus incomplete shunt removal were excluded. Quality assessment was performed with the Newcastle-Ottawa Scale.

Results The search identified 2208 records, of which 8 met the inclusion criteria. All were cohort studies of moderate quality. Four studies compared the duration of antibiotics; none demonstrates that a longer course prevented recurrences. Two studies analysed addition of rifampin, with one showing a decrease in recurrences while the other had a small sample size. No studies analysed the addition of intraventricular antibiotics, but one showed equally good results with once versus twice daily administration. One study reported no difference in recurrences with placement of antibiotic-impregnated catheters. Recurrence rates did not differ with shunt replacement minimum of 7 days vs less than 7 days after CSF became sterile. There were no recurrences in either group when shunt replacement was performed after sterile CSF cultures were obtained at 24 vs 48 hours after antibiotics were discontinued. A new shunt entry site did not decrease recurrences.

Discussion The main limitations are the lack of high-quality studies, the small sample sizes and the heterogeneity which precluded meta-analysis. Addition of rifampin for staphylococcal infections may decrease relapse but requires further study.

Strengths and limitations of this study

- ► There is great heterogeneity in the management of cerebrospinal fluid (CSF) shunt infections, indicating the need for accurate outcomes data.
- ► There are no previous studies that analysed outcomes of more than one intervention for management of CSF shunt infections.
- ► The main limitation is that it was not practical to limit the study to randomised controlled trials.
- ► Only studies published in English or French were included.
- ► Changes in surgical techniques and infection control measures over the 29-year study period might have impacted the outcomes.

INTRODUCTION

Cerebrospinal fluid (CSF) shunt infections impart significant morbidity and occasional mortality in adults and children.[1] Delay in sterilisation of the CSF, relapse (recurrence of infection with the same pathogen as it was not eradicated initially) and reinfection (a new infection, sometimes with a different pathogen) are clearly undesirable outcomes. The Infectious Diseases Society of America (IDSA) guidelines state that the optimal management is removal of the shunt, placement of an external ventricular drain (EVD) and then placement of a new shunt (strong recommendation, moderate quality evidence).[2] However, the optimal choice, duration and route of administration of antibiotics and the optimal timing for replacement of the shunt following CSF sterilisation are not established,[1 2] resulting in significant heterogeneity in management between centres and between neurosurgeons.[3]

A systematic review of studies that compared interventions in patients with CSF shunt infections was performed. The outcomes of interest were (1) time to CSF sterilisation, (2) prevention of relapse and (3) prevention of reinfection.

METHODS

We report our study in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (online supplemental file 1).[4]

Box 1 Medline search strategy:

1. cerebrospinal fluid shunts/ or ventriculoperitoneal shunt/ or ((csf or cerebrospinal fluid or ventriculoperitoneal or ventricle peritoneum) adj shunt*).ti,ab,kf. (12401).
2. exp Bacterial Infections/ or exp Wound Infection/ or (infect* or reinfect* or re-infect*).ti,ab,kf. (2199367).
3. 1 and 2 (2749).
4. exp Anti-Bacterial Agents/ or (anti-bacterial or antibacterial or antibiotic* or anti-biotic* or rifampicin or antibiotic* or vancomycin or tigecylcine or meropenem or gentamicin or linezolid or daptomycin or acetylcysteine or colisin).mp. (913334).
5. exp Injections, Intraventricular/ or exp Infusions, Intraventricular/ or ((Intraventricular or ivt or icv or intracerebroventricular or intracerebro-ventricular or brain ventricle) adj3 (antibiotic* or anti-biotic* or antibacterial or anti-bacterial or infus* or inject* or administ*)).ti,ab,kf. (27852).
6. ((treat* or therap* or manag*) and (infect* or reinfect* or re-infect*)).ti,kf. or ((treat* or therap* or manag*) adj5 (infect* or reinfect* or re-infect*)).ab. (204224).
7. 4 or 5 or 6 (1070585).
8. 3 and 7 (1114).
9. exp Bacterial Infections/dt, su, th [Drug Therapy, Surgery, Therapy] (230287).
10. exp Wound Infection/dt, su, th [Drug Therapy, Surgery, Therapy] (10766).
11. 9 or 10 (237739).
12. 1 and 11 (533).
13. (reimplant* or re-implant* or re-installinstal* or reinstall* or replac* or new shunt*).mp. (456491).
14. 3 and 13 (205).
15. 8 or 12 or 14 (1307).

Ovid Medline and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily (from 1990 to 20 May 2019).

Search strategy

A research librarian conducted a comprehensive literature search in May 2019 (box 1). The search strategy combined subject headings and keywords for cerebrospinal flui shunts, antibiotics and infections. Searches were conducted in the following electronic databases: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid Medline Daily and Ovid Medline, Ovid Embase, Wiley Cochrane Library, CINAHL Plus with Full Text via EBSCOhost, Scopus Advanced Search, and Web of Science Core Collection. The search for records was limited from 1990 to May 2019.

Study selection

The search results were uploaded to EndNote (V.X7; Clarivate Analytics, Philadelphia, Pennsylvania), and all duplicates were removed. Two independent reviewers (JLR, LB) screened the articles for inclusion, first by title and abstract and then by full text. Inclusion criteria were studies of any design that compared treatment-related outcomes with different management strategies in any age group (table 1). Studies were excluded if they were not published in English or French, had five or fewer patients, or if they compared complete with incomplete shunt removal. Although complete removal may not be the optimal strategy for a given patient, it seems highly unlikely that incomplete shunt removal will lead to better infection-related outcomes than will complete removal. Any disagreements with regard to study inclusion were resolved during a consensus meeting.

Definitions

Relapse was defined as a recurrence with the same pathogen (identical genus, species and antimicrobial susceptibilities) within 3 months of antibiotics being stopped.[5] Reinfection was defined as infection with the same or a different pathogen 91 or more days after antibiotics were stopped.

Data extraction

One reviewer developed and piloted a data extraction form in Microsoft Office Excel (V.2016; Microsoft

Table 1 Selection criteria for systematic review of management of cerebrospinal fluid shunt infections

	Inclusion criteria	Exclusion criteria
Study design	► Primary research with a comparison group.	► Reviews. ► Primary research without a comparison group. ► Case reports. ► Guidelines/protocols. ► Opinion pieces including commentaries, editorials and letters.
Setting	► Any study setting.	► None.
Participants/population	► Children and adults.	► None.
Intervention(s), exposure(s)	► Treatments for shunt infections.	► Studies comparing other strategies to removing the entire original infected shunt.
Comparator(s)/control	► Any other management strategy.	► None.
Outcome(s)	► Incidence of infection or reinfection. ► All other outcomes.	► None.
Other	► English or French. ► More than 5 patients.	► All other languages. ► 5 patients or fewer.

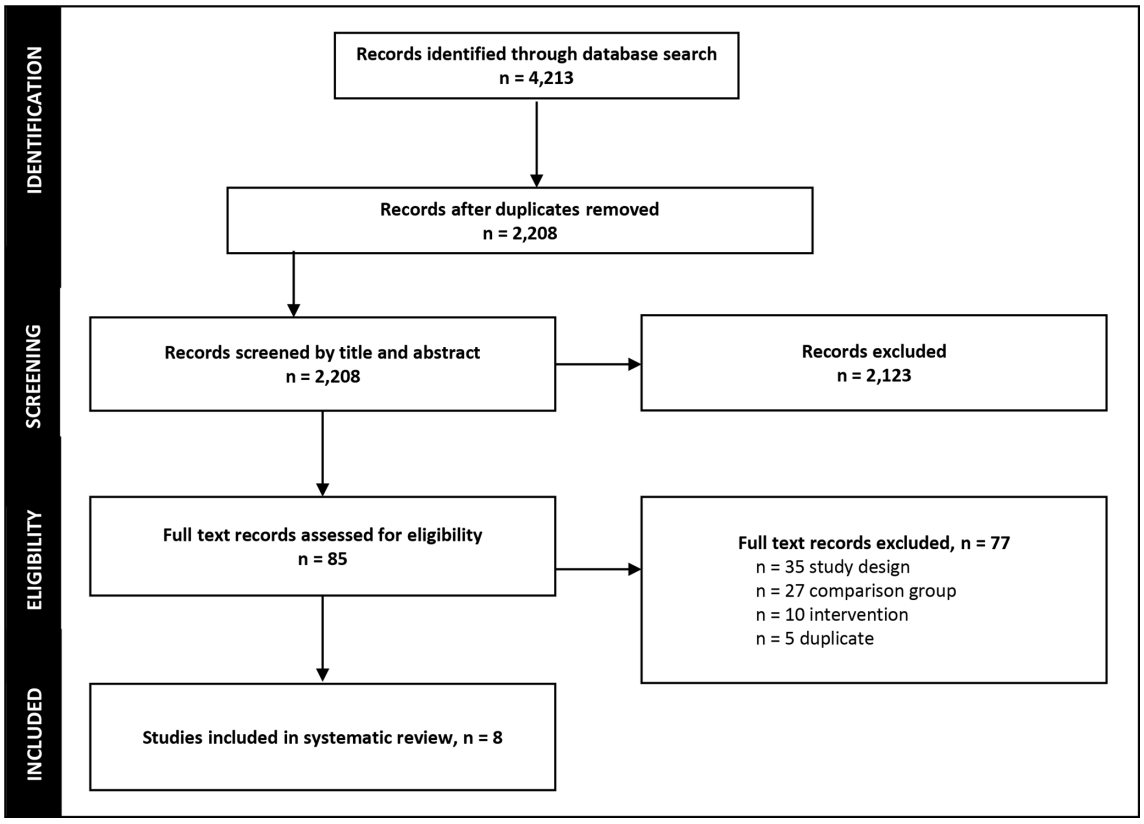

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

Corporation, Redmond, Washington), then extracted data from each included study. A second reviewer verified the data extraction, checking for accuracy and completeness. All disagreements were resolved via discussion.

Quality appraisal

The methodological quality of each included study was assessed using tools tailored to the type of research design. Since all of the included studies were prospective or retrospective cohorts, the Newcastle-Ottawa Scale[6] was used. Each study was awarded an overall star value, up to a maximum of nine stars. All appraisals were completed independently by two reviewers (JLR, DF). Discrepancies were resolved through discussion.

Data synthesis

Because of the heterogeneity of interventions, the primary analysis is narrative.

Patient and public involvement

No patients were involved.

RESULTS

Study selection

We identified 2208 unique records via the search. We screened 85 records by full text, and of these 8 primary studies were eligible for inclusion (figure 1).

Study characteristics

Table 2 describes the included primary studies.[3 5 7–12] All were cohort studies published from 1995 through 2019. Seven studies enrolled children only, while one enrolled adolescents and adults.[10] Data were collected over a minimum of 4 and a maximum of 34 years (table 2). One study analysed delay in CSF sterilisation,[10] while all others analysed recurrence rates. Only one study provided definitions for recurrences due to relapses versus reinfections[5]; however, the authors of that study did not distinguish between relapse and reinfection in the results. Follow-up varied from 6 months[12] to 12 years.[7] Commonly, data were incomplete as the main focus of the study was not the comparison analysed in the current systematic review (table 2).

Adverse events linked to the management strategy were described in only two studies,[7 8] where seizures occurred in 5 of 79 children receiving intraventricular antibiotics two times per day (6%) vs 0 of 33 children receiving them daily. However, one child seized prior to receiving intraventricular antibiotics, and in all cases children continued to receive intraventricular antibiotics with no ongoing seizures.

Study quality

Seven of the cohort studies were retrospective chart reviews, while in the eighth study a database of patients entered prospectively was analysed retrospectively.[9] None of the studies was randomised. The management

Table 2 Characteristics of included studies

First author, year, country	Study design, collection period (initial/historical)	Inclusion criteria	Sample size for this comparison; male,n (%); age (mean±SD)	Description of management (group 1/group 2)	Relapses/reinfections (n) (group 1:group 2)	Duration of follow-up	Implications
James,[7] 2008, USA	Retrospective cohort, 1975–1991 vs 1992–2004	Children from a single centre with monomicrobial CSF-positive shunt infections.	n=40; 21 (53); NR.	Intraventricular antibiotics two times per day* for a total of 1–8 days; intravenous antibiotics given 7–12 days and new shunt placed if CSF sterile with normal parameters 48 hours after antibiotics stopped/same with the exception of intraventricular antibiotics once daily and new shunt placed if CSF sterile with normal parameters 24 hours after antibiotics stopped.	0/25 (0%):0/15 (0%)	'Close follow-up' at 6 months; minimum 1 year; mean 7.7 years in group 1 and 3.3 years in group 2.	Uncomplicated shunt infections can be treated with a total course of 7–12 days of intraventricular and intravenous antibiotics.
James,[8] 2008, USA	Retrospective cohort, 1975–1991 vs 1992–2004	Children from a single centre with polymicrobial shunt infections or multiple compartment formation hydrocephalus.	n=39; 23 (59); NR.	14 days intraventricular antibiotics two times per day and 21 days intravenous antibiotics/same with the exception of intraventricular antibiotics once daily.	0/21 (0%):0/18 (0%)	Routine shunt tap 3–6 months after infection and then followed for a minimum of 1 year.	Complicated shunt infections can be treated with 2 weeks intraventricular (given once daily) and 3 weeks intravenous antibiotics.
Kestle,[9] 2006, USA/Canada	Prospective cohort, May 2001–June 2004	Children under 18 years of age from multiple centres with positive cultures or Gram stain from CSF shunt.	n=66; 35 (50) for 70 in the study; 5.4 (range 26 days–18 years) for 70 in the study.	≤7 days antibiotics once CSF sterile/>7 days antibiotics once CSF sterile.	4/20 (20%):13/46 (28%)	1 year.	An antibiotic course of >7 days following CSF sterilisation does not offer an advantage in a course of ≤7 days.
		Children from the above study with shunt replaced.	n=63; 35 (50) for 70 in the entire cohort; 5.4 (range 26 days–18 years) for 70 in the entire cohort.	New entry site for shunt/same entry site for shunt.	8/35 (23%):8/28 (29%)		A new entry site does not appear to offer significant advantages over using the same entry site.
Pelegrín,[10] 2017,Spain	Retrospective cohort, 1980–2014	Children and adults over 12 years of age from a single centre with CSF-positive shunt infection (or positive shunt tip or wound swab and compatible clinical course).	n=51; 55 (51) for the entire cohort (n=108); median 50 years (IQR 31–70) for the entire cohort (n=108).	Rifampin/no rifampin.	1/7 (14%):16/44 (36%)†	Median 36 weeks.	The sample size was inadequate to analyse efficacy of rifampin in preventing treatment failure.

Continued

Table 2 Continued

First author, year, country	Study design, collection period (initial/historical)	Inclusion criteria	Sample size for this comparison; male,n (%); age (mean±SD)	Description of management (group 1/group 2)	Relapses/reinfections (n) (group 1:group 2)	Duration of follow-up	Implications
Ronan,[5] 1995, Australia	Retrospective cohort, 1981–1991	Children from a single centre with shunt infection, defined as (1) growth from two or more CSFs, (2) growth from one CSF plus compatible Gram stain, (3) culture from CSF identical to that from removed shunt, or (4) positive CSF culture and compatible clinical symptoms at one centre.	n=29; 17 (41) for the entire cohort (n=41); median 1 year for the entire cohort (n=41).	Immediate shunt replacement‡/delayed shunt replacement.	3/7 (43%):1/22 (5%)	Minimum 1 year.	The relapse/reinfection rate is high with immediate shunt replacement.
Simon,[3] 2019, USA/Canada	Retrospective cohort, April 2008–December 2012	Children at sevencentres with initial CSF-positive shunt infection and pathogen addressed in the 2004 IDSA guidelines.	n=124; NR; NR.	Adherence to 2004 guidelines/non-adherence.	0/14 (0%):15/110 (14%)§	Minimum 1 year.	There is no clear evidence that adherence to IDSA guidelines or prolonged courses of antibiotics¶ prevent reinfection, but sample size was small as most management was non-adherent to guidelines.
		Same as above but looked at the 2017 IDSA guidelines.	3/132; NR; NR.	Adherence to 2017 guidelines/non-adherence.	0/3 (0%):18/132 (14%)**		As above.
Simon,[11] 2018, USA	Retrospective cohort, April 2008–December 2012	Children at sevencentres with initial shunt infection meeting the HCRN definition.	n=233; NR; NR.	Rifampin/no rifampin.	2/36 (6%):36/197 (18%)††	Minimum 1 year.	Rifampin reduced the relapse/reinfection rates.
		Same as above.	n=233; NR; NR.	Antibiotic-impregnated shunt placed after initial shunt infection/non-impregnated shunt placedafter initial infection.	8/64 (13%):30/169 (18%)		Antibiotic-impregnated catheters do not appear to decrease relapse/reinfection rates.
Simon,[12] 2010, USA	Retrospective cohort, January 2001–December 2005	Children under 18 years of age with shunt placed in 2001–2005 at 41 children's hospitals, with ICD-9-CM discharge code for shunt infection within 24 months plus another within the subsequent 6 months.	n=675 of which 575 did not get reinfection; 54 of those with reinfection (54); NR.	Duration of antibiotics without reinfections/with reinfections.	Median 6 days (IQR 0–16)/median 7.5 days (IQR 0–17)	6 months.	The duration of antibiotics does not appear to influence the relapse/reinfection rate.

*If <12 months old, serial CSF taps were done in lieu of placing an external ventricular drain, so intraventricular antibiotics were given only when CSF was tapped.
†This study reported on treatment failure rather than relapse/reinfection. For the rifampin data, p=0.421; the patient with reinfection despite rifampin did not have removal of any part of the shunt initially.
‡Not further defined.
§95% CI 0% to 20% recurrence rate in the adherent group vs 8% to 21% in the non-adherent group.
¶9 of 74 children who were treated for longer than recommended (95% CI 6% to 22%) and 2 of 20 who were treated for a shorter time than recommended had reinfection (95% CI 1% to 32%). The other 4 infections were presumably in 16 patients where non-adherence was not related to duration of antibiotics but to timing of placement of new shunt.
**95% CI 0% to 640% recurrence rate in the adherent group vs 8% to 21% in the non-adherent group.
††OR 4.2 (95% CI 1.1 to 27.6) in the full model and 7.9 (95% CI 1.1 to 173.1) if no revisions between the two shunt infections.
CSF, cerebrospinal fluid; HCRN, Hydrocephalus Clinical Research Network; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; IDSA, Infectious Diseases Society of America; NR, not reported.

strategy was presumably at the discretion of the treating clinician in all studies, except for two by the same authors where the routine management strategy changed over time.[7 8] Follow-up for relapses was presumed to be almost complete in all studies as only tertiary care centres would care for patients with shunt infections, so it seems unlikely that the child would be seen at a different centre within 3 months of the end of therapy. However, reinfection can occur years after shunt placement. Based on the Newcastle-Ottawa Scale all studies were of good quality (seven stars) (table 3). The main source of bias in all studies was 'comparability' as it was difficult to establish whether controls and cases had similar characteristics.

Duration of antibiotics

The 2004 and 2017 Infectious Diseases Society of America (IDSA) guidelines specify a suggested duration of antibiotics based on the pathogen and the time to CSF sterilisation.[2] Simon *et al*[3] found no improvement in outcomes with adherence to the guidelines and no evidence that continuing antibiotics beyond the duration indicated in the guidelines prevented recurrences, but the sample size was small; 9 of 74 children (12%) who were treated longer than recommended (95% CI 6% to 22%) and 2 of 20 (10%) who were treated for a shorter time than recommended (95% CI 1% to 32%) developed recurrences. Using the same data set, Simon *et al*[11] reported no difference in recurrences if antibiotics were administered for a total of <7 days, 8–14 days or >14 days (only ORs rather than data are provided).

One study reported a median duration of intravenous antibiotics of 7.5 days (IQR 0–17) in 100 children with recurrences vs 9 days (IQR 0–16) in 575 without recurrences (p=0.98); it is not clear why some children received 0 days of antibiotics as there were no deaths reported.[12] In another study, the mean duration of antibiotics (presumably given intravenously) was 17.4 days in 18 children with recurrences and 16.2 days in the other 52 children; antibiotics were continued for a mean of 14.0 days following CSF sterilisation in 17 cases with recurrences vs 12.7 days in 66 without recurrences.[9] A shorter course of 7–12 days of intravenous antibiotics resulted in cure for 40 children with uncomplicated shunt infections who received concurrent intraventricular antibiotics.[7]

Use of rifampin

One study showed a statistically significant decrease in recurrences in patients treated with rifampin,[11] while another study had too small of a sample size to reach a conclusion on the effect of rifampin on delayed CSF sterilisation (7 patients received rifampin while 44 did not).[10] The analysis in the former study included all pathogens, while it appears that the analysis in the latter study was more appropriately limited to patients with staphylococcal infections (since rifampin is unlikely to cover other pathogens).

Table 3 Study quality assessment using the Newcastle-Ottawa Scale

Author, year	Representativeness of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome of interest not present at start of the study	Comparability of cohorts on the basis of design or analysis (up to two stars)	Assessment of outcome	Long enough follow-up for outcomes to occur	Adequacy of follow-up of cohorts	Total score (maximum 9)
James and Bradley, 2008[7]	Yes	Yes	Yes	Yes	No/unsure	Yes	Yes	Yes	7
James and Bradley, 2008[8]	Yes	Yes	Yes	Yes	No/unsure	Yes	Yes	Yes	7
Kestle *et al*, 2006[9]	Yes	Yes	Yes	Yes	No/unsure	Yes	Yes	Yes	7
Pelegrín *et al*, 2017[10]	Yes	Yes	Yes	Yes	No/unsure	Yes	Yes	Yes	7
Ronan *et al*, 1995[5]	Yes	Yes	Yes	Yes	No/unsure	Yes	Yes	Yes	7
Simon *et al*, 2019[3]	Yes	Yes	Yes	Yes	No/unsure	Yes	Yes	Yes	7
Simon *et al*, 2018[11]	Yes	Yes	Yes	Yes	No/unsure	Yes	Yes	Yes	7
Simon *et al*, 2010[12]	Yes	Yes	Yes	Yes	No/unsure	Yes	Yes	Yes	7

Intraventricular antibiotics

James and Bradley[8] described no relapses or reinfections when intraventricular antibiotics were given once or twice daily for 1–8 days in conjunction with 7–12 days of intravenous antibiotics for uncomplicated shunt infections (monomicrobial infections with a single shunt)[8] or for 21 days with complicated shunt infections. In other studies, 5 of 86 patients[10] and 5 of 41 children[5] were given intraventricular antibiotics. (It is possible that intraventricular antibiotics were given but not mentioned in the other included studies.) Data are not provided, but the authors of one of the studies stated that the rate of recurrences did not differ in those who received intraventricular antibiotics.[5]

Antibiotic-impregnated catheter

Relapse or reinfection occurred in 8 of 64 children (13%) with antibiotic-impregnated catheters placed following an initial infection vs 30 of 169 (18%) without (p>0.05).[11]

Timing of shunt replacement

There were no recurrences in either group when shunt replacement was performed after sterile CSF cultures were obtained at 24 (n=15) vs 48 (n=25) hours after antibiotics were discontinued; negative cultures at 24 hours were considered to be sterile.[7] With daily CSF collection, there was no advantage to waiting 7 days after CSF became sterile to replace the shunt versus waiting a shorter time, but the minimum waiting time prior to shunt replacement was not studied.[9] One study described a higher rate of recurrences with immediate versus delayed shunt replacement (3 of 7 (43%) vs 1 of 22 (5%)),[5] but presumably in the former group they did one-step shunt replacement, which is no longer a recommended strategy.[2]

In one study, the median time from the first culture-positive CSF to shunt replacement was 16 days in cases that led to recurrences vs 13 days in those that did not.[11]

Technique for shunt replacement

Recurrences were reported in 8 of 35 cases (23%) where a new entry site was used for the shunt vs 8 of 28 (29%) where the original site was used (p>0.05).[9]

DISCUSSION

Management of shunt infections is primarily based on expert opinion due to the absence of high-quality studies.[2] The current review found eight studies describing a wide variety of interventions. There did not appear to be a link between the total duration of antibiotics and subsequent recurrences; the minimum duration has not been established. The optimal timing of shunt replacement was not clear, but as one might predict delayed shunt replacement decreased recurrences versus immediate shunt replacement.[5] However, there did not appear to be evidence for waiting beyond documentation of CSF sterilisation to replace the shunt. There were no studies analysing the benefit of adding intraventricular to intravenous antibiotics. Use of rifampin appeared to decrease recurrences, presumably given orally in the setting of staphylococcal infections[11]; the optimal dose and duration are not clear. The IDSA guidelines contain a weak recommendation based on low-quality evidence: 'If the staphylococcal isolate is susceptible to rifampin, this agent may be considered in combination with other antimicrobial agents for staphylococcal ventriculitis and meningitis'.[2] The IDSA guidelines make a strong recommendation (again based on low-quality evidence) that rifampin be added if there is retained intracranial or spinal hardware.[2] Use of rifampin at the time of initial shunt placement warrants further study.

Patients with CSF shunt infection are more prone than others to subsequent infections, as demonstrated by the recurrence rates above 10% in the larger studies in this review.[9–11] A recent Cochrane review reported that when placed initially, antibiotic-impregnated shunts (typically containing clindamycin and rifampin) did not decrease infection rates,[13] but this was based on only one randomised controlled trial (RCT).[14] A subsequent, much larger RCT by Mallucci *et al*[15] demonstrated that antibiotic (but not silver) impregnated shunts decreased infections in initial shunts with a number needed to treat of approximately 25. The only study in the current review that analysed the efficacy of antibiotic-impregnated shunts in preventing recurrences (vs initial infections) was underpowered to show an advantage.[11] In one study, antibiotic-impregnated shunts shifted the pathogens, causing subsequent infections from Gram-positives to Gram-negatives,[16] although another study showed no such effect.[17] The Mallucci *et al* study demonstrated that antibiotic impregnation may prevent Gram-positive but not Gram-negative infections.[15] One study reported a trend towards a higher recurrence rate when antibiotic-impregnated shunts were revised with antibiotic-impregnated components versus components that were not antibiotic-impregnated.[17]

Relapses are due to inadequate surgical or medical therapy of the shunt infection or infection control lapses when the shunt is replaced. Infections typically occur within 3 months of shunt replacement.[5] Reinfection is often attributable to intervening shunt manipulation, but can also be due to factors that are unrelated to the shunt, such as intra-abdominal infection or spontaneous bacterial meningitis.[5] Future studies should attempt to distinguish between relapse and reinfection as it is presumably only relapses that can be prevented by optimal management of a shunt infection. Barriers to categorising infections as relapses versus reinfection are that (1) the upper limit of time after which a recurrence cannot be a relapse is not known (3 months was arbitrarily chosen for the current study as most infections occur within 3 months of shunt placement and this definition was used in a previous study[5]); and (2) early recurrence with the same pathogen (even if confirmed by molecular typing) can be a reinfection rather than a relapse.

The main limitation of this systematic review is the small number of studies, all of which were observational.

Some studies were reasonably large, but the subgroup of patients receiving a given intervention was always relatively small (maximum 64 patients).[11] One confounding factor is that a variety of surgical approaches were used in the studies. The strategy that is now recommended (placement of an EVD followed by replacement of the shunt) was used less in decades past and is still not always practical. Often patients in a given study had inconsistent surgical management. None of the study results distinguished between relapse and reinfection and none reported the timing of recurrences relative to the initial shunt infection. Intervening shunt manipulation is a risk factor for reinfection that was inconsistently described in the studies. Because CSF shunt infections are relatively uncommon, some studies spanned decades. During this time, advances in surgical technique, shunt technology or infection control practices in the operating room and changes in the antibiotics selected[7] could have changed the outcomes. There are many confounding factors that influence the duration of antibiotics prescribed and the timing of shunt replacement. The language limitation might have resulted in exclusion of relevant studies. Although it seems highly unlikely that incomplete shunt removal would lead to less recurrences than would complete shunt removal, inclusion of studies that compared these interventions could have led to an estimate of how many shunts need to be completely removed to prevent one relapse.

The 2017 IDSA guidelines[2] recommend a total course of antibiotics of 10–14 days (but potentially a 21-day course for Gram-negative pathogens). The current study suggests that even 7 days is sufficient in many cases, but does not provide evidence for the optimal duration with specific pathogens. The IDSA guidelines recommend that a new shunt be placed on day 3 after CSF is sterile for coagulase-negative staphylococci infection, on day 7 for *Cutibacterium acnes* (formerly *Propionibacterium acnes*) and on day 10 for all other pathogens.[2] The current study suggests that success can often be achieved with no delay in shunt replacement once CSF is documented to be sterile, but again it does not provide evidence for specific pathogens.

In conclusion, CSF shunt infections are rare and optimal management presumably varies by pathogen. Shunt infections are relatively rare. It is unrealistic to expect that there will soon be adequately powered randomised trials of the choice or duration of antibiotics or of the timing of shunt replacement as such trials would be costly and difficult to organise as they would require participation of a very large number of neurosurgical centres. However, it may be possible to do a randomised trial of addition of rifampin for staphylococcal infections. It seems prudent to advise that pending more data, clinicians follow the 2017 IDSA guidelines[2] in hopes that sufficient data can eventually be collected on failures to allow for optimisation of management. Molecular typing of pathogens from early recurrences should be performed when practical. Given the difficulty in performing RCTs, registries such as the Hydrocephalus Clinical Research Network[11] allow for application of consistent definitions for infection, relapse and reinfection and for comparison of management strategies.

Contributors JLR conceived of the study and designed it, participated in the search, assessed the articles for quality, analysed the data and wrote portions of the first draft of the manuscript. DF performed data extraction, assessed the articles for quality and wrote the first draft of the abstract. LB participated in the search, compared quality assessment results and wrote portions of the first draft of the manuscript.

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Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data sharing not applicable as no datasets generated and/or analysed for this study.

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